(12) UK Patent Application (19) GB (11) 2 385 328 (13) A

(43) Date of A Publication 20.08.2003

(21) Application No 0229456.9

(22) Date of Filing 18.12.2002

(30) Priority Data
(31) 60341988 (32) 19.12.2001 (33) US

(71) Applicant(s)
F Hoffmann-La Roche AG
(Incorporated in Switzerland)
124 Grenzacherstrasse, CH-4070 Basle,
Switzerland

(72) Inventor(s)
Wendy Lea Corbett
Robert Lewis Crowther
Pete William Dunten
R.Ursula Kammlott
Christine Maria Lukacs

(74) Agent and/or Address for Service
Forrester Ketley & Co
Forrester House, 52 Bounds Green Road,
LONDON, N11 2EY, United Kingdom

(51) INT CL[7]
C12N 9/12 , A61K 31/4439 , A61P 3/10 , C07D 417/12
// (C07D 417/12 213:56 277:46)

(52) UK CL (Edition V)
C3H HB7E
C2C CAA
U1S S2413

(56) Documents Cited
Protein Science; Vol 11, pp 2456-2463 (2002).
Tsuge et al.
Structure; Vol 9, pp 205-214 (2001). Ito et al.
Diabetes; Vol 48, pp 1698-1705 (1999).
Mahalingam et al.

(58) Field of Search
INT CL[7] C12N, C30B, G06F
Other: ONLINE: WPI, EPODOC, JAPIO,MEDLINE,
BIOSIS, EMBASE, SCISEARCH, CAPLUS

(54) Abstract Title
Crystals of glucokinase and methods of growing them

(57) Crystalline forms of mammalian Glucokinase of sufficient size and quality to obtain structure data by X-ray crystallography are presented. Methods of growing such crystals are also disclosed.

GB 2 385 328 A

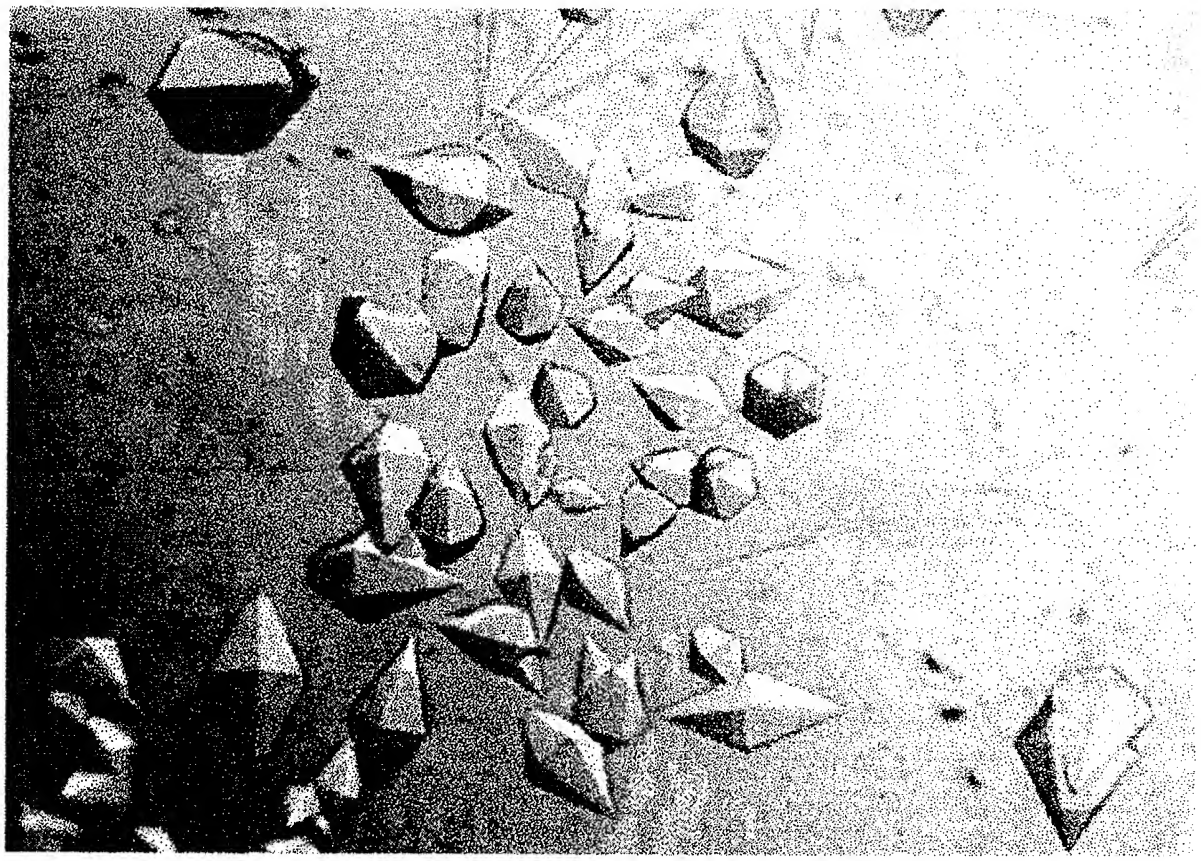


Figure 1

Figure 2. The amino-acid sequence of the GST-GK fusion protein. The GST sequence was taken from GenBank entry U13852. Residue 229 of the fusion protein is the first residue of GK.

```
  1 MSPILGYWKI KGLVQPTRLL LEYLEEKYEE HLYERDEGDK WRNKKFELGL EFPNLPYYID
 61 GDVKLTQSMA IIRYIADKHN MLGGCPKERA EISMLEGAVL DIRYGVSRIA YSKDFETLKV
121 DFLSKLPEML KMFEDRLCHK TYLNGDHVTH PDFMLYDALD VVLYMDPMCL DAFPKLVCFK
181 KRIEAIPQID KYLKSSKYIA WPLQGWQATF GGGDHPPKSD LIEGRGIHMP RPRSQLPQPN
241 SQVEQILAEF QLQEEDLKKV MRRMQKEMDR GLRLETHEEA SVKMLPTYVR STPEGSEVGD
301 FLSLDLGGTN FRVMLVKVGE GEEGQWSVKT KHQMYSIPED AMTGTAEMLF DYISECISDF
361 LDKHQMKHKK LPLGFTFSFP VRHEDIDKGI LLNWTKGFKA SGAEGNNVVG LLRDAIKRRG
421 DFEMDVVAMV NDTVATMISC YYEDHQCEVG MIVGTGCNAC YMEEMQNVEL VEGDEGRMCV
481 NTEWGAFGDS GELDEFLLEY DRLVDESSAN PGQQLYEKLI GGKYMGELVR LVLLRLVDEN
541 LLFHGEASEQ LRTRGAFETR FVSQVESDTG DRKQIYNILS TLGLRPSTTD CDIVRRACES
601 VSTRAAHMCS AGLAGVINRM RESRSEDVMR ITVGVDGSVY KLHPSFKERF HASVRRLTPS
661 CEITFIESEE GSGRGAALVS AVACKKACML GQ
```

Figure 3

Figure 4

Atom No.	Atom Type		A.A. Type	A.A.#	X	Y	Z	OCC	B
ATOM	1	CB	SER	8	-0.421	63.744	24.899	1.00	50.68
ATOM	2	OG	SER	8	-0.752	63.605	23.524	1.00	50.85
ATOM	3	C	SER	8	1.865	64.216	24.094	1.00	50.72
ATOM	4	O	SER	8	2.308	63.644	23.102	1.00	51.79
ATOM	5	N	SER	8	1.473	63.793	26.507	1.00	50.36
ATOM	6	CA	SER	8	1.057	63.446	25.120	1.00	50.55
ATOM	7	N	GLN	9	2.041	65.515	24.314	1.00	49.84
ATOM	8	CA	GLN	9	2.831	66.312	23.385	1.00	48.95
ATOM	9	CB	GLN	9	2.983	67.745	23.895	1.00	49.08
ATOM	10	CG	GLN	9	3.676	68.686	22.925	1.00	50.25
ATOM	11	CD	GLN	9	3.206	70.127	23.085	1.00	51.06
ATOM	12	OE1	GLN	9	2.037	70.433	22.846	1.00	51.38
ATOM	13	NE2	GLN	9	4.112	71.017	23.499	1.00	51.44
ATOM	14	C	GLN	9	4.190	65.633	23.294	1.00	48.56
ATOM	15	O	GLN	9	4.884	65.741	22.285	1.00	48.75
ATOM	16	N	VAL	10	4.560	64.926	24.361	1.00	47.77
ATOM	17	CA	VAL	10	5.823	64.198	24.392	1.00	46.87
ATOM	18	CB	VAL	10	6.293	63.902	25.842	1.00	46.39
ATOM	19	CG1	VAL	10	7.303	62.782	25.841	1.00	46.41
ATOM	20	CG2	VAL	10	6.952	65.135	26.436	1.00	46.79
ATOM	21	C	VAL	10	5.616	62.885	23.653	1.00	46.17
ATOM	22	O	VAL	10	6.521	62.384	22.991	1.00	46.18
ATOM	23	N	GLU	11	4.423	62.317	23.768	1.00	45.28
ATOM	24	CA	GLU	11	4.159	61.071	23.069	1.00	45.19
ATOM	25	CB	GLU	11	2.905	60.393	23.616	1.00	45.21
ATOM	26	CG	GLU	11	3.105	59.709	24.967	1.00	46.05
ATOM	27	CD	GLU	11	4.224	58.664	24.957	1.00	46.30
ATOM	28	OE1	GLU	11	4.350	57.918	23.948	1.00	46.28
ATOM	29	OE2	GLU	11	4.963	58.583	25.972	1.00	45.66
ATOM	30	C	GLU	11	4.002	61.345	21.580	1.00	44.48
ATOM	31	O	GLU	11	4.068	60.430	20.755	1.00	44.48
ATOM	32	N	GLN	12	3.807	62.614	21.239	1.00	43.86
ATOM	33	CA	GLN	12	3.646	62.996	19.845	1.00	42.86
ATOM	34	CB	GLN	12	2.972	64.368	19.715	1.00	44.49
ATOM	35	CG	GLN	12	2.833	64.840	18.259	1.00	46.49
ATOM	36	CD	GLN	12	1.986	66.099	18.113	1.00	47.74
ATOM	37	OE1	GLN	12	2.055	66.799	17.088	1.00	48.30
ATOM	38	NE2	GLN	12	1.174	66.388	19.131	1.00	47.51
ATOM	39	C	GLN	12	5.014	63.023	19.192	1.00	41.14
ATOM	40	O	GLN	12	5.139	62.739	18.002	1.00	41.76
ATOM	41	N	ILE	13	6.038	63.360	19.971	1.00	38.51
ATOM	42	CA	ILE	13	7.398	63.388	19.450	1.00	36.48
ATOM	43	CB	ILE	13	8.274	64.351	20.261	1.00	35.85
ATOM	44	CG2	ILE	13	9.731	64.228	19.827	1.00	35.71
ATOM	45	CG1	ILE	13	7.740	65.777	20.079	1.00	35.77
ATOM	46	CD1	ILE	13	8.584	66.867	20.710	1.00	35.91
ATOM	47	C	ILE	13	8.018	61.981	19.452	1.00	36.01
ATOM	48	O	ILE	13	8.572	61.528	18.442	1.00	35.99
ATOM	49	N	LEU	14	7.903	61.288	20.580	1.00	34.88
ATOM	50	CA	LEU	14	8.430	59.934	20.711	1.00	33.91
ATOM	51	CB	LEU	14	8.230	59.432	22.141	1.00	33.29
ATOM	52	CG	LEU	14	8.853	60.321	23.215	1.00	33.43
ATOM	53	CD1	LEU	14	8.510	59.781	24.594	1.00	33.04
ATOM	54	CD2	LEU	14	10.354	60.398	23.001	1.00	33.04

Figure 4

```
ATOM     55  C   LEU  14       7.766  58.957  19.730  1.00 33.55
ATOM     56  O   LEU  14       8.208  57.812  19.578  1.00 33.21
ATOM     57  N   ALA  15       6.710  59.403  19.065  1.00 32.69
ATOM     58  CA  ALA  15       6.021  58.551  18.104  1.00 32.59
ATOM     59  CB  ALA  15       4.628  59.104  17.821  1.00 31.95
ATOM     60  C   ALA  15       6.838  58.449  16.808  1.00 32.79
ATOM     61  O   ALA  15       6.664  57.519  16.018  1.00 33.05
ATOM     62  N   GLU  16       7.746  59.395  16.599  1.00 32.33
ATOM     63  CA  GLU  16       8.575  59.369  15.403  1.00 32.74
ATOM     64  CB  GLU  16       9.566  60.531  15.401  1.00 34.23
ATOM     65  CG  GLU  16       8.950  61.910  15.298  1.00 38.39
ATOM     66  CD  GLU  16      10.017  62.998  15.162  1.00 41.11
ATOM     67  OE1 GLU  16      10.445  63.269  14.012  1.00 40.68
ATOM     68  OE2 GLU  16      10.438  63.562  16.212  1.00 42.77
ATOM     69  C   GLU  16       9.369  58.073  15.279  1.00 31.93
ATOM     70  O   GLU  16       9.570  57.568  14.179  1.00 33.41
ATOM     71  N   PHE  17       9.841  57.539  16.401  1.00 30.37
ATOM     72  CA  PHE  17      10.640  56.321  16.369  1.00 27.71
ATOM     73  CB  PHE  17      11.346  56.129  17.711  1.00 26.32
ATOM     74  CG  PHE  17      12.309  57.230  18.045  1.00 24.22
ATOM     75  CD1 PHE  17      11.846  58.500  18.389  1.00 23.88
ATOM     76  CD2 PHE  17      13.680  57.010  17.981  1.00 22.24
ATOM     77  CE1 PHE  17      12.741  59.531  18.660  1.00 22.63
ATOM     78  CE2 PHE  17      14.574  58.027  18.250  1.00 21.23
ATOM     79  CZ  PHE  17      14.105  59.291  18.589  1.00 22.01
ATOM     80  C   PHE  17       9.836  55. 004  077  16.012  1.00 27.77
ATOM     81  O   PHE  17      10.400  54. 15.802  1.00 27.38
ATOM     82  N   GLN  18       8.517  55.213  15.957  1.00 28.12
ATOM     83  CA  GLN  18       7.684  54.080  15.593  1.00 29.17
ATOM     84  CB  GLN  18       6.216  54.484  15.599  1.00 30.98
ATOM     85  CG  GLN  18       5.446  54.017  16.806  1.00 32.94
ATOM     86  CD  GLN  18       4.152  54.785  16.974  1.00 34.65
ATOM     87  OE1 GLN  18       3.389  54.976  16.014  1.00 37.17
ATOM     88  NE2 GLN  18       3.892  55.228  18.190  1.00 33.67
ATOM     89  C   GLN  18       8.068  53.602  14.193  1.00 28.97
ATOM     90  O   GLN  18       8.471  54.399  13.346  1.00 28.83
ATOM     91  N   LEU  19       7.931  52.298  13.971  1.00 29.02
ATOM     92  CA  LEU  19       8.235  51.659  12.704  1.00 29.94
ATOM     93  CB  LEU  19       9.641  51.069  12.749  1.00 29.78
ATOM     94  CG  LEU  19      10.782  51.813  12.037  1.00 30.77
ATOM     95  CD1 LEU  19      10.886  53.251  12.477  1.00 30.67
ATOM     96  CD2 LEU  19      12.083  51.087  12.339  1.00 32.05
ATOM     97  C   LEU  19       7.199  50.549  12.511  1.00 31.41
ATOM     98  O   LEU  19       7.288  49.484  13.137  1.00 31.35
ATOM     99  N   GLN  20       6.205  50.801  11.663  1.00 32.64
ATOM    100  CA  GLN  20       5.153  49.817  11.422  1.00 34.95
ATOM    101  CB  GLN  20       4.024  50.413  10.570  1.00 35.78
ATOM    102  CG  GLN  20       3.301  51.622  11.175  1.00 37.65
ATOM    103  CD  GLN  20       3.048  51.486  12.669  1.00 39.03
ATOM    104  OE1 GLN  20       2.603  50.441  13.152  1.00 40.92
ATOM    105  NE2 GLN  20       3.324  52.552  13.410  1.00 40.04
ATOM    106  C   GLN  20       5.692  48.568  10.730  1.00 35.83
ATOM    107  O   GLN  20       6.827  48.547  10.247  1.00 36.56
ATOM    108  N   GLU  21       4.864  47.531  10.681  1.00 36.52
ATOM    109  CA  GLU  21       5.240  46.279  10.062  1.00 37.80
ATOM    110  CB  GLU  21       4.024  45.357   9.998  1.00 39.22
ATOM    111  CG  GLU  21       4.298  43.898   9.625  1.00 42.88
ATOM    112  CD  GLU  21       4.568  43.009  10.844  1.00 44.63
ATOM    113  OE1 GLU  21       4.540  41.758  10.699  1.00 45.40
```

Figure 4

```
ATOM    114  OE2 GLU   21       4.810  43.564  11.943  1.00 45.89
ATOM    115  C   GLU   21       5.770  46.549   8.654  1.00 38.20
ATOM    116  O   GLU   21       6.892  46.183   8.324  1.00 38.71
ATOM    117  N   GLU   22       4.972  47.208   7.826  1.00 38.54
ATOM    118  CA  GLU   22       5.386  47.478   6.457  1.00 39.08
ATOM    119  CB  GLU   22       4.308  48.267   5.703  1.00 40.61
ATOM    120  CG  GLU   22       3.123  47.406   5.313  1.00 43.51
ATOM    121  CD  GLU   22       3.556  46.039   4.773  1.00 45.80
ATOM    122  OE1 GLU   22       4.243  45.999   3.719  1.00 46.20
ATOM    123  OE2 GLU   22       3.215  45.007   5.414  1.00 46.87
ATOM    124  C   GLU   22       6.711  48.197   6.359  1.00 38.74
ATOM    125  O   GLU   22       7.482  47.954   5.423  1.00 39.26
ATOM    126  N   ASP   23       6.988  49.084   7.308  1.00 37.74
ATOM    127  CA  ASP   23       8.258  49.795   7.276  1.00 37.23
ATOM    128  CB  ASP   23       8.356  50.779   8.437  1.00 38.62
ATOM    129  CG  ASP   23       7.240  51.789   8.427  1.00 40.46
ATOM    130  OD1 ASP   23       7.104  52.508   7.408  1.00 41.26
ATOM    131  OD2 ASP   23       6.495  51.861   9.438  1.00 41.77
ATOM    132  C   ASP   23       9.371  48.760   7.382  1.00 35.54
ATOM    133  O   ASP   23      10.267  48.698   6.536  1.00 35.43
ATOM    134  N   LEU   24       9.294  47.937   8.420  1.00 33.31
ATOM    135  CA  LEU   24      10.288  46.910   8.631  1.00 32.04
ATOM    136  CB  LEU   24       9.898  46.062   9.842  1.00 31.35
ATOM    137  CG  LEU   24       9.920  46.801  11.196  1.00 31.20
ATOM    138  CD1 LEU   24       9.710  45.815  12.343  1.00 29.48
ATOM    139  CD2 LEU   24      11.253  47.526  11.367  1.00 31.51
ATOM    140  C   LEU   24      10.509  46.041   7.385  1.00 31.61
ATOM    141  O   LEU   24      11.645  45.723   7.049  1.00 31.67
ATOM    142  N   LYS   25       9.434  45.673   6.693  1.00 31.58
ATOM    143  CA  LYS   25       9.551  44.863   5.486  1.00 31.41
ATOM    144  CB  LYS   25       8.186  44.347   5.061  1.00 31.91
ATOM    145  CG  LYS   25       7.574  43.372   6.033  1.00 34.39
ATOM    146  CD  LYS   25       6.224  42.901   5.531  1.00 36.61
ATOM    147  CE  LYS   25       5.414  42.232   6.640  1.00 38.71
ATOM    148  NZ  LYS   25       3.978  42.086   6.235  1.00 39.39
ATOM    149  C   LYS   25      10.166  45.679   4.352  1.00 31.50
ATOM    150  O   LYS   25      10.969  45.170   3.568  1.00 30.92
ATOM    151  N   LYS   26       9.784  46.947   4.261  1.00 31.82
ATOM    152  CA  LYS   26      10.332  47.819   3.229  1.00 32.63
ATOM    153  CB  LYS   26       9.695  49.203   3.315  1.00 33.38
ATOM    154  CG  LYS   26      10.053  50.129   2.177  1.00 35.11
ATOM    155  CD  LYS   26       9.424  51.502   2.400  1.00 37.48
ATOM    156  CE  LYS   26       9.364  52.312   1.104  1.00 39.72
ATOM    157  NZ  LYS   26       8.706  53.645   1.307  1.00 42.62
ATOM    158  C   LYS   26      11.845  47.919   3.441  1.00 32.91
ATOM    159  O   LYS   26      12.614  48.012   2.479  1.00 32.90
ATOM    160  N   VAL   27      12.265  47.901   4.705  1.00 33.16
ATOM    161  CA  VAL   27      13.687  47.956   5.046  1.00 33.43
ATOM    162  CB  VAL   27      13.903  48.281   6.555  1.00 32.58
ATOM    163  CG1 VAL   27      15.335  47.960   6.963  1.00 32.13
ATOM    164  CG2 VAL   27      13.622  49.755   6.818  1.00 31.04
ATOM    165  C   VAL   27      14.305  46.586   4.727  1.00 33.90
ATOM    166  O   VAL   27      15.323  46.482   4.036  1.00 33.83
ATOM    167  N   MSE   28      13.668  45.536   5.223  1.00 34.26
ATOM    168  CA  MSE   28      14.140  44.193   4.983  1.00 34.84
ATOM    169  CB  MSE   28      13.072  43.198   5.393  1.00 35.83
ATOM    170  CG  MSE   28      13.456  41.784   5.144  1.00 38.88
ATOM    171  SE  MSE   28      12.108  40.670   5.608  1.00 45.40
ATOM    172  CE  MSE   28      11.054  40.713   4.095  1.00 42.96
```

Figure 4

```
ATOM    173  C   MSE  28      14.465  44.016   3.505  1.00 35.32
ATOM    174  O   MSE  28      15.571  43.621   3.144  1.00 35.22
ATOM    175  N   ARG  29      13.495  44.331   2.655  1.00 36.22
ATOM    176  CA  ARG  29      13.665  44.191   1.218  1.00 36.59
ATOM    177  CB  ARG  29      12.352  44.520   0.509  1.00 37.37
ATOM    178  CG  ARG  29      11.223  43.542   0.827  1.00 38.96
ATOM    179  CD  ARG  29       9.913  43.960   0.152  1.00 40.89
ATOM    180  NE  ARG  29       8.760  43.281   0.744  1.00 42.88
ATOM    181  CZ  ARG  29       7.621  43.889   1.081  1.00 43.80
ATOM    182  NH1 ARG  29       7.475  45.201   0.881  1.00 43.07
ATOM    183  NH2 ARG  29       6.631  43.188   1.636  1.00 44.12
ATOM    184  C   ARG  29      14.814  45.008   0.625  1.00 36.30
ATOM    185  O   ARG  29      15.615  44.469  -0.133  1.00 35.58
ATOM    186  N   ARG  30      14.906  46.296   0.948  1.00 36.85
ATOM    187  CA  ARG  30      16.008  47.091   0.410  1.00 38.41
ATOM    188  CB  ARG  30      15.944  48.543   0.894  1.00 39.31
ATOM    189  CG  ARG  30      14.676  49.285   0.513  1.00 41.96
ATOM    190  CD  ARG  30      14.742  50.763   0.933  1.00 44.07
ATOM    191  NE  ARG  30      13.415  51.384   0.995  1.00 45.48
ATOM    192  CZ  ARG  30      13.179  52.628   1.416  1.00 45.93
ATOM    193  NH1 ARG  30      14.175  53.403   1.810  1.00 45.92
ATOM    194  NH2 ARG  30      11.937  53.091   1.467  1.00 45.68
ATOM    195  C   ARG  30      17.338  46.461   0.843  1.00 39.05
ATOM    196  O   ARG  30      18.286  46.404   0.061  1.00 38.99
ATOM    197  N   MSE  31      17.408  45.999   2.092  1.00 39.11
ATOM    198  CA  MSE  31      18.615  45.348   2.596  1.00 38.96
ATOM    199  CB  MSE  31      18.374  44.784   4.002  1.00 40.43
ATOM    200  CG  MSE  31      19.512  43.922   4.599  1.00 42.62
ATOM    201  SE  MSE  31      21.083  44.819   5.027  1.00 48.46
ATOM    202  CE  MSE  31      20.438  45.988   6.389  1.00 45.46
ATOM    203  C   MSE  31      18.901  44.209   1.633  1.00 38.25
ATOM    204  O   MSE  31      19.973  44.132   1.038  1.00 38.18
ATOM    205  N   GLN  32      17.915  43.334   1.478  1.00 37.93
ATOM    206  CA  GLN  32      18.037  42.199   0.589  1.00 37.33
ATOM    207  CB  GLN  32      16.708  41.475   0.480  1.00 36.41
ATOM    208  CG  GLN  32      16.219  40.905   1.780  1.00 37.04
ATOM    209  CD  GLN  32      15.304  39.723   1.561  1.00 37.28
ATOM    210  OE1 GLN  32      15.740  38.682   1.072  1.00 38.23
ATOM    211  NE2 GLN  32      14.027  39.874   1.912  1.00 37.39
ATOM    212  C   GLN  32      18.475  42.641  -0.791  1.00 37.81
ATOM    213  O   GLN  32      19.215  41.929  -1.466  1.00 37.79
ATOM    214  N   LYS  33      18.019  43.819  -1.205  1.00 38.80
ATOM    215  CA  LYS  33      18.362  44.345  -2.516  1.00 39.85
ATOM    216  CB  LYS  33      17.525  45.588  -2.830  1.00 40.63
ATOM    217  CG  LYS  33      17.591  45.992  -4.298  1.00 42.21
ATOM    218  CD  LYS  33      16.924  47.336  -4.561  1.00 43.78
ATOM    219  CE  LYS  33      17.160  47.803  -6.006  1.00 44.42
ATOM    220  NZ  LYS  33      16.639  49.187  -6.256  1.00 44.23
ATOM    221  C   LYS  33      19.843  44.695  -2.574  1.00 40.37
ATOM    222  O   LYS  33      20.519  44.411  -3.564  1.00 40.53
ATOM    223  N   GLU  34      20.331  45.312  -1.500  1.00 40.59
ATOM    224  CA  GLU  34      21.730  45.712  -1.378  1.00 40.95
ATOM    225  CB  GLU  34      21.912  46.641  -0.179  1.00 41.24
ATOM    226  CG  GLU  34      21.229  47.956  -0.359  1.00 41.42
ATOM    227  CD  GLU  34      21.476  48.506  -1.741  1.00 42.21
ATOM    228  OE1 GLU  34      22.650  48.810  -2.063  1.00 42.30
ATOM    229  OE2 GLU  34      20.493  48.613  -2.507  1.00 43.29
ATOM    230  C   GLU  34      22.667  44.528  -1.221  1.00 40.87
ATOM    231  O   GLU  34      23.770  44.527  -1.767  1.00 41.06
```

Figure 4

```
ATOM    232  N   MSE  35      22.233  43.534  -0.456  1.00 41.15
ATOM    233  CA  MSE  35      23.038  42.350  -0.232  1.00 41.36
ATOM    234  CB  MSE  35      22.289  41.354   0.648  1.00 41.62
ATOM    235  CG  MSE  35      22.320  41.711   2.117  1.00 43.28
ATOM    236  SE  MSE  35      21.428  40.506   3.120  1.00 46.51
ATOM    237  CE  MSE  35      22.217  38.947   2.587  1.00 45.63
ATOM    238  C   MSE  35      23.376  41.701  -1.554  1.00 41.91
ATOM    239  O   MSE  35      24.532  41.367  -1.824  1.00 42.73
ATOM    240  N   ASP  36      22.367  41.533  -2.395  1.00 42.15
ATOM    241  CA  ASP  36      22.593  40.898  -3.675  1.00 41.96
ATOM    242  CB  ASP  36      21.264  40.633  -4.369  1.00 43.56
ATOM    243  CG  ASP  36      21.446  39.947  -5.699  1.00 45.91
ATOM    244  OD1 ASP  36      21.821  40.652  -6.675  1.00 46.71
ATOM    245  OD2 ASP  36      21.232  38.707  -5.754  1.00 46.76
ATOM    246  C   ASP  36      23.502  41.717  -4.578  1.00 41.03
ATOM    247  O   ASP  36      24.406  41.178  -5.217  1.00 40.61
ATOM    248  N   ARG  37      23.257  43.021  -4.620  1.00 40.36
ATOM    249  CA  ARG  37      24.034  43.937  -5.446  1.00 39.76
ATOM    250  CB  ARG  37      23.498  45.355  -5.283  1.00 39.56
ATOM    251  CG  ARG  37      22.252  45.621  -6.112  1.00 40.04
ATOM    252  CD  ARG  37      21.465  46.815  -5.590  1.00 41.19
ATOM    253  NE  ARG  37      22.278  48.002  -5.307  1.00 41.70
ATOM    254  CZ  ARG  37      22.938  48.711  -6.221  1.00 42.38
ATOM    255  NH1 ARG  37      22.899  48.362  -7.505  1.00 42.59
ATOM    256  NH2 ARG  37      23.615  49.792  -5.851  1.00 41.94
ATOM    257  C   ARG  37      25.524  43.908  -5.152  1.00 39.94
ATOM    258  O   ARG  37      26.335  43.732  -6.059  1.00 40.39
ATOM    259  N   GLY  38      25.893  44.076  -3.890  1.00 39.94
ATOM    260  CA  GLY  38      27.305  44.063  -3.557  1.00 39.60
ATOM    261  C   GLY  38      27.933  42.689  -3.699  1.00 39.23
ATOM    262  O   GLY  38      29.163  42.546  -3.695  1.00 39.59
ATOM    263  N   LEU  39      27.087  41.677  -3.834  1.00 38.16
ATOM    264  CA  LEU  39      27.545  40.307  -3.960  1.00 37.65
ATOM    265  CB  LEU  39      26.428  39.376  -3.495  1.00 35.76
ATOM    266  CG  LEU  39      26.821  38.029  -2.900  1.00 34.52
ATOM    267  CD1 LEU  39      27.899  38.248  -1.857  1.00 33.52
ATOM    268  CD2 LEU  39      25.606  37.348  -2.284  1.00 32.44
ATOM    269  C   LEU  39      27.931  39.989  -5.407  1.00 39.20
ATOM    270  O   LEU  39      28.594  38.980  -5.681  1.00 39.88
ATOM    271  N   ARG  40      27.537  40.866  -6.329  1.00 40.51
ATOM    272  CA  ARG  40      27.809  40.656  -7.751  1.00 41.77
ATOM    273  CB  ARG  40      26.494  40.686  -8.526  1.00 42.80
ATOM    274  CG  ARG  40      25.735  39.392  -8.377  1.00 44.75
ATOM    275  CD  ARG  40      24.257  39.551  -8.636  1.00 46.47
ATOM    276  NE  ARG  40      23.639  38.239  -8.797  1.00 48.71
ATOM    277  CZ  ARG  40      22.331  38.034  -8.890  1.00 50.01
ATOM    278  NH1 ARG  40      21.497  39.064  -8.831  1.00 51.43
ATOM    279  NH2 ARG  40      21.861  36.804  -9.060  1.00 50.46
ATOM    280  C   ARG  40      28.802  41.623  -8.374  1.00 42.16
ATOM    281  O   ARG  40      28.783  42.819  -8.097  1.00 42.42
ATOM    282  N   LEU  41      29.650  41.087  -9.247  1.00 42.03
ATOM    283  CA  LEU  41      30.689  41.864  -9.902  1.00 42.00
ATOM    284  CB  LEU  41      31.307  41.044 -11.041  1.00 42.00
ATOM    285  CG  LEU  41      32.577  41.650 -11.660  1.00 41.78
ATOM    286  CD1 LEU  41      33.638  41.836 -10.583  1.00 40.20
ATOM    287  CD2 LEU  41      33.087  40.747 -12.773  1.00 41.95
ATOM    288  C   LEU  41      30.278  43.237 -10.428  1.00 42.57
ATOM    289  O   LEU  41      30.920  44.243 -10.110  1.00 42.64
ATOM    290  N   GLU  42      29.219  43.292 -11.227  1.00 43.03
```

Figure 4

```
ATOM    291  CA  GLU    42      28.788  44.562 -11.803  1.00 44.63
ATOM    292  CB  GLU    42      27.494  44.369 -12.607  1.00 43.97
ATOM    293  CG  GLU    42      26.436  43.533 -11.922  1.00 44.02
ATOM    294  CD  GLU    42      26.546  42.057 -12.248  1.00 43.71
ATOM    295  OE1 GLU    42      27.673  41.527 -12.245  1.00 45.13
ATOM    296  OE2 GLU    42      25.504  41.416 -12.496  1.00 43.50
ATOM    297  C   GLU    42      28.616  45.714 -10.805  1.00 46.21
ATOM    298  O   GLU    42      28.963  46.860 -11.103  1.00 46.22
ATOM    299  N   THR    43      28.105  45.413  -9.616  1.00 47.90
ATOM    300  CA  THR    43      27.873  46.443  -8.608  1.00 49.10
ATOM    301  CB  THR    43      26.370  46.533  -8.285  1.00 48.63
ATOM    302  OG1 THR    43      25.772  45.242  -8.465  1.00 47.66
ATOM    303  CG2 THR    43      25.679  47.531  -9.192  1.00 48.90
ATOM    304  C   THR    43      28.629  46.226  -7.302  1.00 50.94
ATOM    305  O   THR    43      28.481  47.008  -6.362  1.00 51.52
ATOM    306  N   HIS    44      29.456  45.185  -7.249  1.00 52.58
ATOM    307  CA  HIS    44      30.204  44.854  -6.037  1.00 53.89
ATOM    308  CB  HIS    44      31.210  43.727  -6.311  1.00 54.68
ATOM    309  CG  HIS    44      32.552  44.208  -6.775  1.00 55.77
ATOM    310  CD2 HIS    44      33.748  44.257  -6.139  1.00 55.82
ATOM    311  ND1 HIS    44      32.758  44.772  -8.017  1.00 56.36
ATOM    312  CE1 HIS    44      34.020  45.146  -8.125  1.00 56.30
ATOM    313  NE2 HIS    44      34.643  44.845  -6.999  1.00 56.06
ATOM    314  C   HIS    44      30.950  46.013  -5.398  1.00 54.87
ATOM    315  O   HIS    44      30.823  46.254  -4.199  1.00 55.06
ATOM    316  N   GLU    45      31.724  46.732  -6.203  1.00 56.25
ATOM    317  CA  GLU    45      32.540  47.826  -5.703  1.00 57.17
ATOM    318  CB  GLU    45      33.618  48.180  -6.721  1.00 59.35
ATOM    319  CG  GLU    45      33.146  49.127  -7.800  1.00 61.61
ATOM    320  CD  GLU    45      34.107  50.279  -7.985  1.00 63.07
ATOM    321  OE1 GLU    45      35.228  50.038  -8.487  1.00 63.72
ATOM    322  OE2 GLU    45      33.747  51.420  -7.613  1.00 64.00
ATOM    323  C   GLU    45      31.762  49.074  -5.356  1.00 56.66
ATOM    324  O   GLU    45      32.295  49.985  -4.732  1.00 56.54
ATOM    325  N   GLU    46      30.508  49.135  -5.772  1.00 56.24
ATOM    326  CA  GLU    46      29.708  50.306  -5.456  1.00 56.37
ATOM    327  CB  GLU    46      29.542  51.157  -6.704  1.00 57.92
ATOM    328  CG  GLU    46      30.881  51.645  -7.212  1.00 60.77
ATOM    329  CD  GLU    46      30.782  52.400  -8.515  1.00 62.28
ATOM    330  OE1 GLU    46      30.566  51.762  -9.571  1.00 62.25
ATOM    331  OE2 GLU    46      30.914  53.641  -8.474  1.00 63.95
ATOM    332  C   GLU    46      28.366  49.891  -4.873  1.00 55.40
ATOM    333  O   GLU    46      27.309  50.123  -5.457  1.00 55.75
ATOM    334  N   ALA    47      28.440  49.264  -3.704  1.00 53.89
ATOM    335  CA  ALA    47      27.273  48.783  -2.987  1.00 51.80
ATOM    336  CB  ALA    47      27.140  47.280  -3.159  1.00 52.36
ATOM    337  C   ALA    47      27.470  49.111  -1.524  1.00 49.98
ATOM    338  O   ALA    47      28.448  48.664  -0.923  1.00 50.36
ATOM    339  N   SER    48      26.553  49.894  -0.960  1.00 47.18
ATOM    340  CA  SER    48      26.630  50.267   0.444  1.00 44.70
ATOM    341  CB  SER    48      25.299  50.860   0.897  1.00 46.13
ATOM    342  OG  SER    48      24.243  49.927   0.720  1.00 47.87
ATOM    343  C   SER    48      26.965  49.041   1.287  1.00 42.45
ATOM    344  O   SER    48      27.841  49.082   2.147  1.00 42.01
ATOM    345  N   VAL    49      26.261  47.946   1.037  1.00 40.48
ATOM    346  CA  VAL    49      26.516  46.713   1.762  1.00 38.96
ATOM    347  CB  VAL    49      25.231  45.849   1.875  1.00 38.62
ATOM    348  CG1 VAL    49      25.496  44.625   2.740  1.00 38.40
ATOM    349  CG2 VAL    49      24.102  46.672   2.472  1.00 37.16
```

Figure 4

```
ATOM    350  C   VAL  49      27.572  45.997   0.929  1.00 37.97
ATOM    351  O   VAL  49      27.266  45.474  -0.137  1.00 38.42
ATOM    352  N   LYS  50      28.810  45.982   1.422  1.00 36.51
ATOM    353  CA  LYS  50      29.937  45.385   0.703  1.00 34.95
ATOM    354  CB  LYS  50      31.250  45.843   1.334  1.00 35.51
ATOM    355  CG  LYS  50      31.574  47.322   1.091  1.00 36.68
ATOM    356  CD  LYS  50      30.676  48.249   1.913  1.00 39.05
ATOM    357  CE  LYS  50      30.865  48.018   3.419  1.00 39.54
ATOM    358  NZ  LYS  50      32.316  48.157   3.792  1.00 40.04
ATOM    359  C   LYS  50      30.012  43.879   0.482  1.00 33.72
ATOM    360  O   LYS  50      30.845  43.421  -0.293  1.00 33.30
ATOM    361  N   MSE  51      29.171  43.100   1.147  1.00 33.02
ATOM    362  CA  MSE  51      29.209  41.647   0.967  1.00 32.08
ATOM    363  CB  MSE  51      28.291  41.257  -0.190  1.00 34.01
ATOM    364  CG  MSE  51      26.867  41.744  -0.025  1.00 36.83
ATOM    365  SE  MSE  51      26.148  41.146   1.529  1.00 40.73
ATOM    366  CE  MSE  51      25.558  39.411   1.085  1.00 37.98
ATOM    367  C   MSE  51      30.637  41.180   0.666  1.00 30.17
ATOM    368  O   MSE  51      30.928  40.723  -0.437  1.00 30.22
ATOM    369  N   LEU  52      31.518  41.295   1.650  1.00 28.96
ATOM    370  CA  LEU  52      32.920  40.928   1.487  1.00 27.43
ATOM    371  CB  LEU  52      33.769  41.839   2.357  1.00 28.05
ATOM    372  CG  LEU  52      33.649  43.319   1.991  1.00 28.52
ATOM    373  CD1 LEU  52      34.222  44.171   3.116  1.00 28.77
ATOM    374  CD2 LEU  52      34.369  43.583   0.658  1.00 28.75
ATOM    375  C   LEU  52      33.273  39.482   1.803  1.00 26.61
ATOM    376  O   LEU  52      32.997  38.995   2.893  1.00 25.26
ATOM    377  N   PRO  53      33.911  38.774   0.844  1.00 27.04
ATOM    378  CD  PRO  53      34.270  39.142  -0.540  1.00 25.69
ATOM    379  CA  PRO  53      34.264  37.375   1.133  1.00 27.99
ATOM    380  CB  PRO  53      34.807  36.864  -0.204  1.00 26.92
ATOM    381  CG  PRO  53      34.184  37.825  -1.241  1.00 25.77
ATOM    382  C   PRO  53      35.314  37.361   2.239  1.00 28.40
ATOM    383  O   PRO  53      36.152  38.271   2.317  1.00 28.36
ATOM    384  N   THR  54      35.255  36.329   3.080  1.00 29.46
ATOM    385  CA  THR  54      36.149  36.142   4.226  1.00 30.53
ATOM    386  CB  THR  54      35.317  35.951   5.502  1.00 29.48
ATOM    387  OG1 THR  54      34.589  34.711   5.418  1.00 27.97
ATOM    388  CG2 THR  54      34.324  37.084   5.659  1.00 29.42
ATOM    389  C   THR  54      37.018  34.884   4.071  1.00 31.60
ATOM    390  O   THR  54      37.657  34.423   5.025  1.00 32.25
ATOM    391  N   TYR  55      37.017  34.311   2.877  1.00 32.63
ATOM    392  CA  TYR  55      37.763  33.089   2.615  1.00 34.41
ATOM    393  CB  TYR  55      39.249  33.421   2.405  1.00 33.07
ATOM    394  CG  TYR  55      39.458  34.175   1.101  1.00 32.58
ATOM    395  CD1 TYR  55      39.518  35.571   1.067  1.00 32.44
ATOM    396  CE1 TYR  55      39.572  36.263  -0.157  1.00 32.48
ATOM    397  CD2 TYR  55      39.467  33.492  -0.117  1.00 31.97
ATOM    398  CE2 TYR  55      39.516  34.172  -1.335  1.00 31.83
ATOM    399  CZ  TYR  55      39.566  35.548  -1.351  1.00 32.18
ATOM    400  OH  TYR  55      39.575  36.200  -2.568  1.00 32.67
ATOM    401  C   TYR  55      37.559  31.956   3.637  1.00 36.06
ATOM    402  O   TYR  55      38.314  30.991   3.665  1.00 37.61
ATOM    403  N   VAL  56      36.518  32.059   4.459  1.00 38.03
ATOM    404  CA  VAL  56      36.199  31.006   5.429  1.00 39.87
ATOM    405  CB  VAL  56      35.483  31.586   6.663  1.00 38.75
ATOM    406  CG1 VAL  56      35.202  30.492   7.669  1.00 38.10
ATOM    407  CG2 VAL  56      36.336  32.660   7.285  1.00 38.76
ATOM    408  C   VAL  56      35.249  30.032   4.706  1.00 42.20
```

Figure 4

```
ATOM    409  O   VAL    56      34.098  30.376   4.418  1.00 42.02
ATOM    410  N   ARG    57      35.718  28.821   4.414  1.00 44.49
ATOM    411  CA  ARG    57      34.896  27.860   3.676  1.00 47.07
ATOM    412  CB  ARG    57      35.688  27.288   2.499  1.00 48.02
ATOM    413  CG  ARG    57      36.209  28.310   1.508  1.00 49.08
ATOM    414  CD  ARG    57      36.558  27.626   0.185  1.00 49.69
ATOM    415  NE  ARG    57      37.239  28.528  -0.737  1.00 49.50
ATOM    416  CZ  ARG    57      38.367  29.167  -0.447  1.00 48.83
ATOM    417  NH1 ARG    57      38.938  28.997   0.745  1.00 48.13
ATOM    418  NH2 ARG    57      38.915  29.978  -1.345  1.00 47.51
ATOM    419  C   ARG    57      34.311  26.695   4.449  1.00 48.57
ATOM    420  O   ARG    57      34.810  26.310   5.500  1.00 48.65
ATOM    421  N   SER    58      33.256  26.117   3.891  1.00 51.15
ATOM    422  CA  SER    58      32.589  24.973   4.501  1.00 54.78
ATOM    423  CB  SER    58      31.204  24.793   3.882  1.00 54.26
ATOM    424  OG  SER    58      31.258  24.980   2.475  1.00 54.39
ATOM    425  C   SER    58      33.419  23.708   4.295  1.00 57.39
ATOM    426  O   SER    58      33.097  22.645   4.823  1.00 57.47
ATOM    427  N   THR    59      34.484  23.840   3.510  1.00 60.71
ATOM    428  CA  THR    59      35.392  22.740   3.216  1.00 64.02
ATOM    429  CB  THR    59      35.886  22.823   1.758  1.00 63.73
ATOM    430  OG1 THR    59      36.637  24.029   1.570  1.00 63.22
ATOM    431  CG2 THR    59      34.704  22.843   0.801  1.00 63.87
ATOM    432  C   THR    59      36.571  22.880   4.176  1.00 67.10
ATOM    433  O   THR    59      37.554  23.562   3.884  1.00 67.44
ATOM    434  N   PRO    60      36.480  22.238   5.349  1.00 69.75
ATOM    435  CD  PRO    60      35.366  21.412   5.854  1.00 70.63
ATOM    436  CA  PRO    60      37.556  22.320   6.337  1.00 71.72
ATOM    437  CB  PRO    60      36.841  21.982   7.636  1.00 71.72
ATOM    438  CG  PRO    60      35.909  20.881   7.182  1.00 71.50
ATOM    439  C   PRO    60      38.709  21.370   6.056  1.00 73.48
ATOM    440  O   PRO    60      39.522  21.609   5.158  1.00 73.53
ATOM    441  N   GLU    61      38.754  20.287   6.830  1.00 75.48
ATOM    442  CA  GLU    61      39.808  19.283   6.731  1.00 76.98
ATOM    443  CB  GLU    61      39.969  18.788   5.289  1.00 78.43
ATOM    444  CG  GLU    61      40.806  17.516   5.161  1.00 80.68
ATOM    445  CD  GLU    61      42.177  17.744   4.530  1.00 81.88
ATOM    446  OE1 GLU    61      42.993  18.498   5.100  1.00 82.28
ATOM    447  OE2 GLU    61      42.442  17.156   3.458  1.00 82.68
ATOM    448  C   GLU    61      41.083  19.969   7.194  1.00 77.00
ATOM    449  O   GLU    61      41.942  20.327   6.389  1.00 77.10
ATOM    450  N   GLY    62      41.177  20.181   8.502  1.00 76.85
ATOM    451  CA  GLY    62      42.344  20.826   9.069  1.00 76.72
ATOM    452  C   GLY    62      42.415  20.539  10.555  1.00 76.65
ATOM    453  O   GLY    62      42.507  19.380  10.969  1.00 76.79
ATOM    454  N   SER    63      42.361  21.594  11.362  1.00 76.25
ATOM    455  CA  SER    63      42.417  21.458  12.814  1.00 75.06
ATOM    456  CB  SER    63      41.401  20.413  13.300  1.00 75.92
ATOM    457  OG  SER    63      41.350  20.363  14.718  1.00 76.69
ATOM    458  C   SER    63      43.818  21.062  13.259  1.00 73.60
ATOM    459  O   SER    63      44.090  19.899  13.561  1.00 73.10
ATOM    460  N   GLU    64      44.705  22.045  13.280  1.00 71.83
ATOM    461  CA  GLU    64      46.071  21.819  13.703  1.00 70.12
ATOM    462  CB  GLU    64      46.996  22.824  13.011  1.00 71.42
ATOM    463  CG  GLU    64      48.464  22.726  13.417  1.00 73.74
ATOM    464  CD  GLU    64      49.014  21.309  13.342  1.00 74.84
ATOM    465  OE1 GLU    64      48.623  20.466  14.187  1.00 75.26
ATOM    466  OE2 GLU    64      49.837  21.041  12.434  1.00 75.45
ATOM    467  C   GLU    64      46.136  21.971  15.221  1.00 67.97
```

Figure 4

```
ATOM    468  O   GLU  64      46.775  22.886  15.734  1.00 68.33
ATOM    469  N   VAL  65      45.448  21.076  15.927  1.00 65.13
ATOM    470  CA  VAL  65      45.400  21.067  17.391  1.00 62.32
ATOM    471  CB  VAL  65      45.335  19.621  17.918  1.00 62.48
ATOM    472  CG1 VAL  65      45.487  19.607  19.430  1.00 62.45
ATOM    473  CG2 VAL  65      44.011  18.975  17.508  1.00 62.79
ATOM    474  C   VAL  65      46.587  21.752  18.055  1.00 60.42
ATOM    475  O   VAL  65      47.703  21.708  17.540  1.00 60.54
ATOM    476  N   GLY  66      46.354  22.386  19.200  1.00 58.26
ATOM    477  CA  GLY  66      47.454  23.043  19.888  1.00 55.67
ATOM    478  C   GLY  66      47.081  24.174  20.823  1.00 53.42
ATOM    479  O   GLY  66      46.153  24.052  21.615  1.00 54.08
ATOM    480  N   ASP  67      47.832  25.267  20.739  1.00 51.06
ATOM    481  CA  ASP  67      47.614  26.460  21.549  1.00 48.67
ATOM    482  CB  ASP  67      48.617  26.531  22.703  1.00 49.14
ATOM    483  CG  ASP  67      48.381  25.462  23.751  1.00 49.34
ATOM    484  OD1 ASP  67      48.201  24.287  23.365  1.00 49.37
ATOM    485  OD2 ASP  67      48.386  25.791  24.956  1.00 49.62
ATOM    486  C   ASP  67      47.832  27.634  20.612  1.00 47.26
ATOM    487  O   ASP  67      48.786  27.635  19.827  1.00 47.44
ATOM    488  N   PHE  68      46.955  28.632  20.678  1.00 45.41
ATOM    489  CA  PHE  68      47.075  29.778  19.785  1.00 43.60
ATOM    490  CB  PHE  68      46.031  29.682  18.667  1.00 41.17
ATOM    491  CG  PHE  68      46.032  28.361  17.946  1.00 39.29
ATOM    492  CD1 PHE  68      45.621  27.199  18.592  1.00 38.55
ATOM    493  CD2 PHE  68      46.468  28.272  16.623  1.00 38.76
ATOM    494  CE1 PHE  68      45.647  25.966  17.934  1.00 38.24
ATOM    495  CE2 PHE  68      46.498  27.050  15.959  1.00 37.31
ATOM    496  CZ  PHE  68      46.086  25.893  16.619  1.00 37.76
ATOM    497  C   PHE  68      46.918  31.096  20.514  1.00 43.33
ATOM    498  O   PHE  68      46.395  31.147  21.621  1.00 43.27
ATOM    499  N   LEU  69      47.386  32.166  19.889  1.00 43.51
ATOM    500  CA  LEU  69      47.274  33.475  20.497  1.00 44.73
ATOM    501  CB  LEU  69      48.625  34.197  20.518  1.00 45.26
ATOM    502  CG  LEU  69      48.781  34.949  21.848  1.00 46.33
ATOM    503  CD1 LEU  69      49.166  33.928  22.932  1.00 46.09
ATOM    504  CD2 LEU  69      49.811  36.072  21.748  1.00 45.48
ATOM    505  C   LEU  69      46.275  34.278  19.681  1.00 45.37
ATOM    506  O   LEU  69      46.448  34.451  18.470  1.00 45.62
ATOM    507  N   SER  70      45.228  34.758  20.351  1.00 45.75
ATOM    508  CA  SER  70      44.177  35.528  19.697  1.00 44.98
ATOM    509  CB  SER  70      42.794  34.984  20.074  1.00 44.61
ATOM    510  OG  SER  70      42.697  33.589  19.844  1.00 44.25
ATOM    511  C   SER  70      44.250  36.978  20.109  1.00 44.92
ATOM    512  O   SER  70      44.451  37.289  21.277  1.00 44.67
ATOM    513  N   LEU  71      44.095  37.858  19.130  1.00 45.85
ATOM    514  CA  LEU  71      44.092  39.294  19.366  1.00 47.27
ATOM    515  CB  LEU  71      45.064  40.000  18.421  1.00 47.71
ATOM    516  CG  LEU  71      46.552  39.942  18.787  1.00 49.06
ATOM    517  CD1 LEU  71      47.008  38.497  19.039  1.00 49.69
ATOM    518  CD2 LEU  71      47.348  40.572  17.656  1.00 49.35
ATOM    519  C   LEU  71      42.668  39.752  19.082  1.00 47.94
ATOM    520  O   LEU  71      41.873  38.997  18.499  1.00 48.06
ATOM    521  N   ASP  72      42.333  40.976  19.479  1.00 48.20
ATOM    522  CA  ASP  72      40.985  41.451  19.244  1.00 48.67
ATOM    523  CB  ASP  72      40.043  40.807  20.262  1.00 48.71
ATOM    524  CG  ASP  72      38.668  41.420  20.243  1.00 49.13
ATOM    525  OD1 ASP  72      38.090  41.549  19.144  1.00 49.57
ATOM    526  OD2 ASP  72      38.168  41.777  21.331  1.00 50.11
```

Figure 4

	ATOM	527	C	ASP	72	40.819	42.962	19.258	1.00	48.98
	ATOM	528	O	ASP	72	40.247	43.530	20.187	1.00	48.82
	ATOM	529	N	LEU	73	41.312	43.613	18.214	1.00	49.73
	ATOM	530	CA	LEU	73	41.193	45.060	18.117	1.00	51.48
5	ATOM	531	CB	LEU	73	42.199	45.603	17.096	1.00	50.80
	ATOM	532	CG	LEU	73	42.160	47.096	16.774	1.00	50.07
	ATOM	533	CD1	LEU	73	42.358	47.902	18.045	1.00	50.10
	ATOM	534	CD2	LEU	73	43.223	47.421	15.738	1.00	49.97
	ATOM	535	C	LEU	73	39.764	45.392	17.687	1.00	52.93
10	ATOM	536	O	LEU	73	38.909	44.507	17.628	1.00	52.38
	ATOM	537	N	GLY	74	39.504	46.665	17.401	1.00	54.88
	ATOM	538	CA	GLY	74	38.177	47.068	16.983	1.00	56.88
	ATOM	539	C	GLY	74	37.285	47.420	18.148	1.00	58.48
	ATOM	540	O	GLY	74	36.476	48.348	18.071	1.00	58.31
15	ATOM	541	N	GLY	75	37.428	46.668	19.233	1.00	60.27
	ATOM	542	CA	GLY	75	36.621	46.925	20.410	1.00	62.46
	ATOM	543	C	GLY	75	37.020	48.230	21.074	1.00	63.75
	ATOM	544	O	GLY	75	37.824	49.005	20.536	1.00	64.06
	ATOM	545	N	THR	76	36.452	48.481	22.248	1.00	64.50
20	ATOM	546	CA	THR	76	36.759	49.697	22.991	1.00	65.42
	ATOM	547	CB	THR	76	35.905	49.776	24.266	1.00	66.28
	ATOM	548	OG1	THR	76	36.361	48.791	25.203	1.00	67.43
	ATOM	549	CG2	THR	76	34.425	49.505	23.938	1.00	66.14
	ATOM	550	C	THR	76	38.238	49.651	23.385	1.00	65.25
25	ATOM	551	O	THR	76	39.005	50.595	23.152	1.00	65.01
	ATOM	552	N	ASN	77	38.622	48.528	23.980	1.00	64.74
	ATOM	553	CA	ASN	77	39.987	48.309	24.412	1.00	64.17
	ATOM	554	CB	ASN	77	40.015	47.966	25.903	1.00	65.44
	ATOM	555	CG	ASN	77	39.346	49.027	26.765	1.00	66.47
30	ATOM	556	OD1	ASN	77	39.656	50.219	26.663	1.00	67.13
	ATOM	557	ND2	ASN	77	38.431	48.596	27.629	1.00	66.65
	ATOM	558	C	ASN	77	40.547	47.149	23.603	1.00	63.19
	ATOM	559	O	ASN	77	39.795	46.303	23.120	1.00	62.58
	ATOM	560	N	PHE	78	41.866	47.123	23.446	1.00	62.14
35	ATOM	561	CA	PHE	78	42.526	46.051	22.708	1.00	61.12
	ATOM	562	CB	PHE	78	43.887	46.514	22.172	1.00	61.81
	ATOM	563	CG	PHE	78	44.684	45.420	21.516	1.00	62.50
	ATOM	564	CD1	PHE	78	44.347	44.956	20.245	1.00	62.81
	ATOM	565	CD2	PHE	78	45.741	44.818	22.189	1.00	62.99
40	ATOM	566	CE1	PHE	78	45.051	43.899	19.655	1.00	62.72
	ATOM	567	CE2	PHE	78	46.450	43.763	21.607	1.00	63.38
	ATOM	568	CZ	PHE	78	46.103	43.301	20.336	1.00	63.01
	ATOM	569	C	PHE	78	42.732	44.893	23.668	1.00	60.09
	ATOM	570	O	PHE	78	43.065	45.100	24.834	1.00	60.08
45	ATOM	571	N	ARG	79	42.528	43.675	23.184	1.00	58.63
	ATOM	572	CA	ARG	79	42.706	42.504	24.025	1.00	57.40
	ATOM	573	CB	ARG	79	41.367	41.819	24.280	1.00	57.06
	ATOM	574	CG	ARG	79	41.481	40.637	25.222	1.00	57.49
	ATOM	575	CD	ARG	79	40.221	39.819	25.219	1.00	57.47
50	ATOM	576	NE	ARG	79	39.062	40.646	25.504	1.00	57.16
	ATOM	577	CZ	ARG	79	37.818	40.266	25.267	1.00	57.69
	ATOM	578	NH1	ARG	79	37.586	39.071	24.738	1.00	57.38
	ATOM	579	NH2	ARG	79	36.812	41.080	25.555	1.00	58.45
	ATOM	580	C	ARG	79	43.663	41.522	23.368	1.00	56.71
55	ATOM	581	O	ARG	79	43.926	41.619	22.170	1.00	57.24
	ATOM	582	N	VAL	80	44.180	40.590	24.167	1.00	55.50
	ATOM	583	CA	VAL	80	45.114	39.557	23.724	1.00	54.27
	ATOM	584	CB	VAL	80	46.576	39.947	23.996	1.00	54.31
	ATOM	585	CG1	VAL	80	47.491	38.779	23.674	1.00	54.49

Figure 4

```
ATOM    586  CG2 VAL    80      46.960  41.158  23.166  1.00 54.39
ATOM    587  C   VAL    80      44.806  38.327  24.555  1.00 54.04
ATOM    588  O   VAL    80      44.517  38.447  25.738  1.00 53.31
ATOM    589  N   MSE    81      44.881  37.144  23.957  1.00 54.52
ATOM    590  CA  MSE    81      44.568  35.935  24.703  1.00 54.59
ATOM    591  CB  MSE    81      43.053  35.804  24.828  1.00 57.08
ATOM    592  CG  MSE    81      42.300  36.025  23.520  1.00 60.39
ATOM    593  SE  MSE    81      40.534  36.437  23.792  1.00 65.62
ATOM    594  CE  MSE    81      39.999  34.926  24.679  1.00 62.03
ATOM    595  C   MSE    81      45.142  34.645  24.146  1.00 53.56
ATOM    596  O   MSE    81      45.598  34.582  23.007  1.00 52.99
ATOM    597  N   LEU    82      45.096  33.611  24.978  1.00 52.63
ATOM    598  CA  LEU    82      45.602  32.292  24.638  1.00 51.86
ATOM    599  CB  LEU    82      46.660  31.863  25.665  1.00 52.75
ATOM    600  CG  LEU    82      47.261  30.455  25.542  1.00 53.22
ATOM    601  CD1 LEU    82      48.562  30.521  24.736  1.00 52.42
ATOM    602  CD2 LEU    82      47.523  29.882  26.937  1.00 53.00
ATOM    603  C   LEU    82      44.461  31.286  24.650  1.00 51.18
ATOM    604  O   LEU    82      43.718  31.186  25.632  1.00 51.20
ATOM    605  N   VAL    83      44.333  30.535  23.563  1.00 50.58
ATOM    606  CA  VAL    83      43.292  29.522  23.448  1.00 50.00
ATOM    607  CB  VAL    83      42.274  29.887  22.362  1.00 49.63
ATOM    608  CG1 VAL    83      41.213  28.794  22.262  1.00 49.26
ATOM    609  CG2 VAL    83      41.660  31.244  22.670  1.00 48.32
ATOM    610  C   VAL    83      43.914  28.187  23.080  1.00 50.53
ATOM    611  O   VAL    83      44.759  28.122  22.192  1.00 50.93
ATOM    612  N   LYS    84      43.496  27.127  23.763  1.00 51.05
ATOM    613  CA  LYS    84      44.017  25.788  23.504  1.00 51.89
ATOM    614  CB  LYS    84      44.338  25.061  24.826  1.00 51.79
ATOM    615  CG  LYS    84      44.716  23.581  24.659  1.00 51.85
ATOM    616  CD  LYS    84      44.951  22.870  26.009  1.00 51.58
ATOM    617  CE  LYS    84      46.429  22.848  26.422  1.00 50.92
ATOM    618  NZ  LYS    84      47.041  24.198  26.592  1.00 50.33
ATOM    619  C   LYS    84      42.997  24.983  22.708  1.00 52.68
ATOM    620  O   LYS    84      42.115  24.327  23.282  1.00 53.00
ATOM    621  N   VAL    85      43.124  25.038  21.383  1.00 52.91
ATOM    622  CA  VAL    85      42.224  24.319  20.488  1.00 52.70
ATOM    623  CB  VAL    85      42.399  24.805  19.048  1.00 51.79
ATOM    624  CG1 VAL    85      41.302  24.232  18.176  1.00 52.19
ATOM    625  CG2 VAL    85      42.389  26.319  19.017  1.00 51.59
ATOM    626  C   VAL    85      42.525  22.823  20.548  1.00 53.51
ATOM    627  O   VAL    85      43.637  22.389  20.243  1.00 53.87
ATOM    628  N   GLY    86      41.534  22.037  20.952  1.00 54.38
ATOM    629  CA  GLY    86      41.726  20.603  21.053  1.00 55.35
ATOM    630  C   GLY    86      40.901  19.810  20.060  1.00 56.21
ATOM    631  O   GLY    86      40.136  20.370  19.278  1.00 55.63
ATOM    632  N   GLU    87      41.050  18.493  20.106  1.00 57.81
ATOM    633  CA  GLU    87      40.339  17.611  19.195  1.00 59.64
ATOM    634  CB  GLU    87      41.290  16.529  18.673  1.00 60.88
ATOM    635  CG  GLU    87      40.680  15.648  17.611  1.00 62.26
ATOM    636  CD  GLU    87      40.215  16.457  16.423  1.00 63.21
ATOM    637  OE1 GLU    87      41.072  16.931  15.644  1.00 63.20
ATOM    638  OE2 GLU    87      38.989  16.631  16.278  1.00 64.58
ATOM    639  C   GLU    87      39.133  16.959  19.859  1.00 60.12
ATOM    640  O   GLU    87      39.271  16.187  20.810  1.00 60.00
ATOM    641  N   GLY    88      37.948  17.273  19.347  1.00 60.93
ATOM    642  CA  GLY    88      36.735  16.707  19.902  1.00 61.61
ATOM    643  C   GLY    88      35.840  16.120  18.833  1.00 62.11
ATOM    644  O   GLY    88      36.038  16.346  17.638  1.00 61.67
```

Figure 4

```
ATOM    645  N   GLU  89      34.845  15.363  19.274  1.00 62.79
ATOM    646  CA  GLU  89      33.898  14.724  18.372  1.00 63.90
ATOM    647  CB  GLU  89      32.782  14.089  19.203  1.00 63.50
ATOM    648  CG  GLU  89      33.304  13.137  20.275  1.00 62.64
ATOM    649  CD  GLU  89      32.214  12.623  21.203  1.00 62.46
ATOM    650  OE1 GLU  89      32.510  11.728  22.019  1.00 62.39
ATOM    651  OE2 GLU  89      31.064  13.110  21.128  1.00 62.11
ATOM    652  C   GLU  89      33.312  15.688  17.325  1.00 65.16
ATOM    653  O   GLU  89      32.975  16.837  17.634  1.00 64.98
ATOM    654  N   GLU  90      33.204  15.205  16.087  1.00 66.03
ATOM    655  CA  GLU  90      32.667  15.977  14.958  1.00 66.67
ATOM    656  CB  GLU  90      31.135  15.974  14.978  1.00 67.21
ATOM    657  CG  GLU  90      30.495  14.620  14.717  1.00 66.83
ATOM    658  CD  GLU  90      28.986  14.662  14.869  1.00 67.49
ATOM    659  OE1 GLU  90      28.308  15.273  14.009  1.00 67.17
ATOM    660  OE2 GLU  90      28.480  14.090  15.858  1.00 66.84
ATOM    661  C   GLU  90      33.149  17.421  14.871  1.00 66.91
ATOM    662  O   GLU  90      32.623  18.212  14.080  1.00 66.74
ATOM    663  N   GLY  91      34.149  17.769  15.671  1.00 67.05
ATOM    664  CA  GLY  91      34.649  19.126  15.628  1.00 67.38
ATOM    665  C   GLY  91      36.036  19.339  16.201  1.00 67.42
ATOM    666  O   GLY  91      37.025  18.797  15.708  1.00 68.24
ATOM    667  N   GLN  92      36.094  20.154  17.246  1.00 66.86
ATOM    668  CA  GLN  92      37.335  20.492  17.929  1.00 65.93
ATOM    669  CB  GLN  92      38.395  20.968  16.924  1.00 66.17
ATOM    670  CG  GLN  92      38.007  22.215  16.159  1.00 66.24
ATOM    671  CD  GLN  92      38.564  22.236  14.750  1.00 66.57
ATOM    672  OE1 GLN  92      38.432  21.260  14.007  1.00 66.37
ATOM    673  NE2 GLN  92      39.177  23.356  14.367  1.00 66.54
ATOM    674  C   GLN  92      36.999  21.605  18.920  1.00 65.21
ATOM    675  O   GLN  92      36.625  22.721  18.530  1.00 65.44
ATOM    676  N   TRP  93      37.111  21.278  20.204  1.00 63.62
ATOM    677  CA  TRP  93      36.820  22.227  21.261  1.00 61.61
ATOM    678  CB  TRP  93      36.859  21.540  22.626  1.00 62.77
ATOM    679  CG  TRP  93      38.050  20.641  22.857  1.00 63.86
ATOM    680  CD2 TRP  93      39.213  20.943  23.637  1.00 64.17
ATOM    681  CE2 TRP  93      40.026  19.787  23.645  1.00 64.21
ATOM    682  CE3 TRP  93      39.647  22.080  24.336  1.00 64.11
ATOM    683  CD1 TRP  93      38.206  19.349  22.424  1.00 63.84
ATOM    684  NE1 TRP  93      39.387  18.830  22.897  1.00 63.69
ATOM    685  CZ2 TRP  93      41.246  19.731  24.324  1.00 64.43
ATOM    686  CZ3 TRP  93      40.859  22.026  25.009  1.00 64.63
ATOM    687  CH2 TRP  93      41.645  20.857  24.999  1.00 64.71
ATOM    688  C   TRP  93      37.784  23.393  21.248  1.00 59.53
ATOM    689  O   TRP  93      38.733  23.420  20.474  1.00 59.18
ATOM    690  N   SER  94      37.521  24.366  22.106  1.00 57.94
ATOM    691  CA  SER  94      38.353  25.549  22.207  1.00 56.46
ATOM    692  CB  SER  94      37.880  26.615  21.219  1.00 56.58
ATOM    693  OG  SER  94      36.504  26.899  21.412  1.00 56.78
ATOM    694  C   SER  94      38.185  26.050  23.624  1.00 55.56
ATOM    695  O   SER  94      37.142  25.822  24.237  1.00 55.36
ATOM    696  N   VAL  95      39.208  26.722  24.146  1.00 54.53
ATOM    697  CA  VAL  95      39.152  27.248  25.504  1.00 53.17
ATOM    698  CB  VAL  95      39.511  26.183  26.549  1.00 52.17
ATOM    699  CG1 VAL  95      39.742  26.844  27.891  1.00 52.13
ATOM    700  CG2 VAL  95      38.396  25.172  26.666  1.00 51.73
ATOM    701  C   VAL  95      40.099  28.399  25.719  1.00 52.74
ATOM    702  O   VAL  95      41.268  28.315  25.357  1.00 53.14
ATOM    703  N   LYS  96      39.587  29.469  26.318  1.00 52.63
```

Figure 4

ATOM	704	CA	LYS	96	40.402	30.637	26.629	1.00	52.93
ATOM	705	CB	LYS	96	39.513	31.849	26.932	1.00	53.25
ATOM	706	CG	LYS	96	40.277	33.129	27.231	1.00	53.79
ATOM	707	CD	LYS	96	39.910	33.706	28.595	1.00	54.80
ATOM	708	CE	LYS	96	38.427	34.102	28.682	1.00	55.69
ATOM	709	NZ	LYS	96	38.027	35.162	27.696	1.00	55.59
ATOM	710	C	LYS	96	41.154	30.218	27.882	1.00	52.96
ATOM	711	O	LYS	96	40.546	29.733	28.834	1.00	52.93
ATOM	712	N	THR	97	42.470	30.384	27.886	1.00	53.38
ATOM	713	CA	THR	97	43.253	29.980	29.050	1.00	53.93
ATOM	714	CB	THR	97	44.238	28.850	28.684	1.00	53.99
ATOM	715	OG1	THR	97	43.512	27.736	28.151	1.00	52.99
ATOM	716	CG2	THR	97	44.998	28.394	29.918	1.00	55.29
ATOM	717	C	THR	97	44.036	31.132	29.670	1.00	53.82
ATOM	718	O	THR	97	44.330	31.123	30.866	1.00	53.84
ATOM	719	N	LYS	98	44.373	32.117	28.848	1.00	53.85
ATOM	720	CA	LYS	98	45.115	33.276	29.315	1.00	54.60
ATOM	721	CB	LYS	98	46.627	33.096	29.087	1.00	55.51
ATOM	722	CG	LYS	98	47.220	31.809	29.652	1.00	56.78
ATOM	723	CD	LYS	98	47.074	31.733	31.162	1.00	58.23
ATOM	724	CE	LYS	98	47.553	30.389	31.713	1.00	58.82
ATOM	725	NZ	LYS	98	47.404	30.320	33.201	1.00	58.98
ATOM	726	C	LYS	98	44.644	34.479	28.518	1.00	54.54
ATOM	727	O	LYS	98	44.323	34.360	27.329	1.00	54.79
ATOM	728	N	HIS	99	44.590	35.632	29.173	1.00	54.03
ATOM	729	CA	HIS	99	44.193	36.853	28.496	1.00	54.03
ATOM	730	CB	HIS	99	42.720	36.793	28.052	1.00	55.02
ATOM	731	CG	HIS	99	41.732	36.872	29.172	1.00	55.71
ATOM	732	CD2	HIS	99	40.682	37.704	29.373	1.00	55.66
ATOM	733	ND1	HIS	99	41.739	35.999	30.239	1.00	56.19
ATOM	734	CE1	HIS	99	40.736	36.288	31.049	1.00	56.30
ATOM	735	NE2	HIS	99	40.080	37.319	30.546	1.00	56.72
ATOM	736	C	HIS	99	44.445	38.082	29.351	1.00	53.46
ATOM	737	O	HIS	99	44.526	38.007	30.577	1.00	53.47
ATOM	738	N	GLN	100	44.583	39.214	28.683	1.00	52.94
ATOM	739	CA	GLN	100	44.841	40.468	29.349	1.00	53.34
ATOM	740	CB	GLN	100	46.354	40.649	29.513	1.00	53.39
ATOM	741	CG	GLN	100	46.790	42.001	30.055	1.00	54.26
ATOM	742	CD	GLN	100	46.168	42.345	31.394	1.00	54.43
ATOM	743	OE1	GLN	100	46.349	41.629	32.384	1.00	55.27
ATOM	744	NE2	GLN	100	45.433	43.452	31.432	1.00	53.60
ATOM	745	C	GLN	100	44.243	41.567	28.481	1.00	53.43
ATOM	746	O	GLN	100	44.416	41.569	27.260	1.00	53.75
ATOM	747	N	THR	101	43.527	42.493	29.105	1.00	52.90
ATOM	748	CA	THR	101	42.905	43.576	28.367	1.00	53.12
ATOM	749	CB	THR	101	41.495	43.826	28.894	1.00	52.52
ATOM	750	OG1	THR	101	40.789	42.582	28.925	1.00	52.85
ATOM	751	CG2	THR	101	40.752	44.808	27.999	1.00	52.23
ATOM	752	C	THR	101	43.731	44.845	28.499	1.00	53.61
ATOM	753	O	THR	101	44.285	45.108	29.563	1.00	53.95
ATOM	754	N	TYR	102	43.809	45.628	27.422	1.00	54.10
ATOM	755	CA	TYR	102	44.585	46.869	27.422	1.00	55.36
ATOM	756	CB	TYR	102	45.878	46.708	26.608	1.00	54.89
ATOM	757	CG	TYR	102	46.788	45.569	27.015	1.00	54.25
ATOM	758	CD1	TYR	102	46.382	44.241	26.888	1.00	54.08
ATOM	759	CE1	TYR	102	47.227	43.197	27.226	1.00	53.44
ATOM	760	CD2	TYR	102	48.069	45.822	27.497	1.00	53.79
ATOM	761	CE2	TYR	102	48.922	44.785	27.840	1.00	53.76
ATOM	762	CZ	TYR	102	48.498	43.475	27.701	1.00	53.85

Figure 4

```
ATOM    763  OH  TYR  102      49.355  42.442  28.021  1.00 54.03
ATOM    764  C   TYR  102      43.813  48.041  26.822  1.00 56.65
ATOM    765  O   TYR  102      43.173  47.899  25.781  1.00 56.91
ATOM    766  N   SER  103      43.891  49.203  27.462  1.00 58.50
ATOM    767  CA  SER  103      43.217  50.385  26.938  1.00 60.94
ATOM    768  CB  SER  103      42.997  51.411  28.049  1.00 61.09
ATOM    769  OG  SER  103      44.231  51.829  28.602  1.00 62.50
ATOM    770  C   SER  103      44.090  50.985  25.833  1.00 62.31
ATOM    771  O   SER  103      45.293  50.729  25.771  1.00 62.27
ATOM    772  N   ALA  104      43.487  51.783  24.960  1.00 64.47
ATOM    773  CA  ALA  104      44.226  52.386  23.856  1.00 67.01
ATOM    774  CB  ALA  104      43.516  52.093  22.526  1.00 67.01
ATOM    775  C   ALA  104      44.410  53.888  24.025  1.00 68.66
ATOM    776  O   ALA  104      43.458  54.658  23.902  1.00 69.01
ATOM    777  N   PRO  105      45.648  54.327  24.305  1.00 70.09
ATOM    778  CD  PRO  105      46.878  53.522  24.397  1.00 70.06
ATOM    779  CA  PRO  105      45.946  55.751  24.485  1.00 71.25
ATOM    780  CB  PRO  105      47.443  55.748  24.783  1.00 70.79
ATOM    781  CG  PRO  105      47.929  54.535  24.046  1.00 70.54
ATOM    782  C   PRO  105      45.592  56.586  23.251  1.00 72.81
ATOM    783  O   PRO  105      45.837  56.170  22.117  1.00 73.09
ATOM    784  N   GLU  106      45.012  57.762  23.479  1.00 74.39
ATOM    785  CA  GLU  106      44.619  58.652  22.391  1.00 76.25
ATOM    786  CB  GLU  106      43.991  59.921  22.950  1.00 76.77
ATOM    787  CG  GLU  106      42.702  59.673  23.680  1.00 78.35
ATOM    788  CD  GLU  106      42.397  60.775  24.657  1.00 79.28
ATOM    789  OE1 GLU  106      42.239  61.934  24.214  1.00 79.74
ATOM    790  OE2 GLU  106      42.326  60.478  25.871  1.00 80.03
ATOM    791  C   GLU  106      45.784  59.028  21.494  1.00 77.33
ATOM    792  O   GLU  106      45.600  59.262  20.300  1.00 77.48
ATOM    793  N   ASP  107      46.980  59.104  22.068  1.00 78.72
ATOM    794  CA  ASP  107      48.161  59.440  21.284  1.00 80.10
ATOM    795  CB  ASP  107      49.431  59.316  22.134  1.00 80.44
ATOM    796  CG  ASP  107      49.965  57.889  22.185  1.00 81.03
ATOM    797  OD1 ASP  107      49.198  56.976  22.569  1.00 81.42
ATOM    798  OD2 ASP  107      51.151  57.682  21.839  1.00 80.86
ATOM    799  C   ASP  107      48.212  58.424  20.151  1.00 80.92
ATOM    800  O   ASP  107      48.724  58.703  19.065  1.00 81.29
ATOM    801  N   ALA  108      47.670  57.241  20.428  1.00 81.68
ATOM    802  CA  ALA  108      47.628  56.151  19.463  1.00 82.45
ATOM    803  CB  ALA  108      47.605  54.813  20.200  1.00 82.45
ATOM    804  C   ALA  108      46.406  56.275  18.553  1.00 82.91
ATOM    805  O   ALA  108      46.536  56.351  17.331  1.00 82.98
ATOM    806  N   MSE  109      45.221  56.303  19.157  1.00 83.41
ATOM    807  CA  MSE  109      43.974  56.414  18.407  1.00 83.78
ATOM    808  CB  MSE  109      42.787  56.519  19.368  1.00 85.45
ATOM    809  CG  MSE  109      41.581  55.678  18.972  1.00 87.01
ATOM    810  SE  MSE  109      41.933  53.898  19.096  1.00 90.12
ATOM    811  CE  MSE  109      42.665  53.581  17.453  1.00 88.95
ATOM    812  C   MSE  109      43.992  57.633  17.494  1.00 83.17
ATOM    813  O   MSE  109      43.235  57.710  16.527  1.00 83.19
ATOM    814  N   THR  110      44.854  58.590  17.820  1.00 82.51
ATOM    815  CA  THR  110      44.986  59.815  17.040  1.00 82.00
ATOM    816  CB  THR  110      45.289  61.022  17.949  1.00 82.44
ATOM    817  OG1 THR  110      44.302  61.103  18.986  1.00 83.00
ATOM    818  CG2 THR  110      45.283  62.313  17.142  1.00 82.69
ATOM    819  C   THR  110      46.150  59.640  16.082  1.00 81.25
ATOM    820  O   THR  110      46.127  60.123  14.949  1.00 80.95
ATOM    821  N   GLY  111      47.168  58.933  16.559  1.00 80.84
```

Figure 4

```
ATOM    822  CA  GLY  111      48.358  58.691  15.768  1.00 80.12
ATOM    823  C   GLY  111      48.121  57.986  14.450  1.00 79.53
ATOM    824  O   GLY  111      47.018  57.531  14.148  1.00 79.54
ATOM    825  N   THR  112      49.181  57.904  13.658  1.00 78.87
ATOM    826  CA  THR  112      49.129  57.254  12.360  1.00 78.09
ATOM    827  CB  THR  112      50.427  57.553  11.561  1.00 78.67
ATOM    828  OG1 THR  112      50.329  57.001  10.240  1.00 79.18
ATOM    829  CG2 THR  112      51.644  56.956  12.279  1.00 78.48
ATOM    830  C   THR  112      48.992  55.748  12.579  1.00 77.09
ATOM    831  O   THR  112      49.231  55.254  13.685  1.00 76.48
ATOM    832  N   ALA  113      48.601  55.027  11.529  1.00 76.26
ATOM    833  CA  ALA  113      48.443  53.573  11.603  1.00 75.60
ATOM    834  CB  ALA  113      48.184  53.001  10.208  1.00 76.00
ATOM    835  C   ALA  113      49.711  52.965  12.191  1.00 74.65
ATOM    836  O   ALA  113      49.665  52.006  12.968  1.00 74.58
ATOM    837  N   GLU  114      50.845  53.538  11.803  1.00 73.24
ATOM    838  CA  GLU  114      52.139  53.088  12.288  1.00 71.57
ATOM    839  CB  GLU  114      53.246  53.971  11.700  1.00 72.34
ATOM    840  CG  GLU  114      53.130  54.167  10.188  1.00 71.64
ATOM    841  CD  GLU  114      53.325  52.877   9.401  1.00 72.49
ATOM    842  OE1 GLU  114      53.192  51.781   9.994  1.00 72.24
ATOM    843  OE2 GLU  114      53.600  52.960   8.183  1.00 71.83
ATOM    844  C   GLU  114      52.085  53.233  13.801  1.00 70.37
ATOM    845  O   GLU  114      52.297  52.266  14.537  1.00 69.92
ATOM    846  N   MET  115      51.778  54.450  14.246  1.00 68.75
ATOM    847  CA  MET  115      51.657  54.760  15.669  1.00 66.97
ATOM    848  CB  MET  115      51.013  56.140  15.866  1.00 67.15
ATOM    849  CG  MET  115      51.999  57.277  16.040  1.00 66.94
ATOM    850  SD  MET  115      53.203  56.869  17.320  1.00 67.61
ATOM    851  CE  MET  115      52.137  56.732  18.788  1.00 66.65
ATOM    852  C   MET  115      50.799  53.718  16.374  1.00 65.81
ATOM    853  O   MET  115      51.266  53.010  17.275  1.00 65.94
ATOM    854  N   LEU  116      49.542  53.635  15.940  1.00 63.70
ATOM    855  CA  LEU  116      48.561  52.711  16.504  1.00 61.63
ATOM    856  CB  LEU  116      47.287  52.720  15.650  1.00 60.89
ATOM    857  CG  LEU  116      45.948  52.226  16.205  1.00 59.42
ATOM    858  CD1 LEU  116      44.953  52.182  15.051  1.00 58.84
ATOM    859  CD2 LEU  116      46.081  50.858  16.847  1.00 58.86
ATOM    860  C   LEU  116      49.083  51.285  16.613  1.00 60.35
ATOM    861  O   LEU  116      48.977  50.665  17.667  1.00 60.48
ATOM    862  N   PHE  117      49.641  50.756  15.531  1.00 59.14
ATOM    863  CA  PHE  117      50.138  49.391  15.580  1.00 58.14
ATOM    864  CB  PHE  117      50.298  48.819  14.173  1.00 57.03
ATOM    865  CG  PHE  117      49.055  48.144  13.669  1.00 56.22
ATOM    866  CD1 PHE  117      48.005  48.889  13.143  1.00 55.49
ATOM    867  CD2 PHE  117      48.909  46.763  13.783  1.00 55.59
ATOM    868  CE1 PHE  117      46.830  48.270  12.741  1.00 55.25
ATOM    869  CE2 PHE  117      47.736  46.134  13.384  1.00 55.20
ATOM    870  CZ  PHE  117      46.695  46.887  12.862  1.00 55.23
ATOM    871  C   PHE  117      51.415  49.204  16.382  1.00 57.89
ATOM    872  O   PHE  117      51.799  48.073  16.690  1.00 57.80
ATOM    873  N   ALA  118      52.078  50.303  16.725  1.00 57.35
ATOM    874  CA  ALA  118      53.275  50.193  17.537  1.00 56.79
ATOM    875  CB  ALA  118      54.004  51.533  17.594  1.00 56.42
ATOM    876  C   ALA  118      52.747  49.792  18.922  1.00 56.46
ATOM    877  O   ALA  118      53.220  48.829  19.536  1.00 56.68
ATOM    878  N   ALA  119      51.733  50.515  19.391  1.00 55.57
ATOM    879  CA  ALA  119      51.142  50.226  20.693  1.00 55.05
ATOM    880  CB  ALA  119      49.931  51.135  20.952  1.00 53.91
```

Figure 4

```
ATOM    881  C   ALA  119      50.719  48.769  20.763  1.00 54.96
ATOM    882  O   ALA  119      51.090  48.052  21.698  1.00 54.94
ATOM    883  N   ILE  120      49.948  48.338  19.763  1.00 55.10
ATOM    884  CA  ILE  120      49.443  46.969  19.715  1.00 55.51
ATOM    885  CB  ILE  120      48.679  46.679  18.397  1.00 54.45
ATOM    886  CG2 ILE  120      47.922  45.363  18.525  1.00 53.30
ATOM    887  CG1 ILE  120      47.688  47.808  18.089  1.00 53.32
ATOM    888  CD1 ILE  120      46.871  47.581  16.820  1.00 51.70
ATOM    889  C   ILE  120      50.575  45.957  19.846  1.00 56.57
ATOM    890  O   ILE  120      50.477  45.006  20.632  1.00 56.52
ATOM    891  N   SER  121      51.645  46.169  19.076  1.00 57.78
ATOM    892  CA  SER  121      52.814  45.284  19.093  1.00 58.54
ATOM    893  CB  SER  121      53.844  45.730  18.045  1.00 58.96
ATOM    894  OG  SER  121      53.377  45.507  16.720  1.00 59.32
ATOM    895  C   SER  121      53.457  45.280  20.473  1.00 58.74
ATOM    896  O   SER  121      54.007  44.265  20.918  1.00 57.56
ATOM    897  N   GLU  122      53.379  46.422  21.151  1.00 59.50
ATOM    898  CA  GLU  122      53.947  46.529  22.484  1.00 60.44
ATOM    899  CB  GLU  122      54.003  47.986  22.941  1.00 60.60
ATOM    900  CG  GLU  122      55.104  48.241  23.952  1.00 60.45
ATOM    901  CD  GLU  122      54.706  49.252  25.003  1.00 61.76
ATOM    902  OE1 GLU  122      54.152  50.312  24.630  1.00 61.92
ATOM    903  OE2 GLU  122      54.950  48.986  26.202  1.00 62.20
ATOM    904  C   GLU  122      53.091  45.725  23.452  1.00 60.63
ATOM    905  O   GLU  122      53.565  44.761  24.048  1.00 60.82
ATOM    906  N   CYS  123      51.831  46.120  23.605  1.00 60.96
ATOM    907  CA  CYS  123      50.936  45.410  24.510  1.00 61.79
ATOM    908  CB  CYS  123      49.481  45.840  24.278  1.00 61.63
ATOM    909  SG  CYS  123      49.191  47.636  24.439  1.00 62.83
ATOM    910  C   CYS  123      51.107  43.922  24.233  1.00 61.90
ATOM    911  O   CYS  123      51.028  43.095  25.147  1.00 61.89
ATOM    912  N   ILE  124      51.350  43.588  22.966  1.00 62.36
ATOM    913  CA  ILE  124      51.561  42.197  22.588  1.00 62.79
ATOM    914  CB  ILE  124      52.033  42.061  21.109  1.00 62.52
ATOM    915  CG2 ILE  124      52.618  40.676  20.877  1.00 61.07
ATOM    916  CG1 ILE  124      50.866  42.280  20.138  1.00 61.53
ATOM    917  CD1 ILE  124      50.016  41.038  19.888  1.00 61.77
ATOM    918  C   ILE  124      52.673  41.706  23.499  1.00 62.76
ATOM    919  O   ILE  124      52.475  40.807  24.320  1.00 62.23
ATOM    920  N   SER  125      53.839  42.327  23.347  1.00 63.43
ATOM    921  CA  SER  125      55.020  42.002  24.138  1.00 64.63
ATOM    922  CB  SER  125      56.062  43.117  23.986  1.00 65.05
ATOM    923  OG  SER  125      57.324  42.745  24.523  1.00 67.01
ATOM    924  C   SER  125      54.646  41.840  25.610  1.00 64.32
ATOM    925  O   SER  125      54.886  40.794  26.219  1.00 64.46
ATOM    926  N   ASP  126      54.047  42.884  26.169  1.00 64.43
ATOM    927  CA  ASP  126      53.626  42.894  27.562  1.00 64.86
ATOM    928  CB  ASP  126      52.660  44.060  27.788  1.00 64.95
ATOM    929  CG  ASP  126      52.390  44.323  29.253  1.00 65.38
ATOM    930  OD1 ASP  126      51.952  43.389  29.955  1.00 65.74
ATOM    931  OD2 ASP  126      52.613  45.467  29.706  1.00 65.92
ATOM    932  C   ASP  126      52.968  41.572  27.980  1.00 64.65
ATOM    933  O   ASP  126      53.424  40.918  28.924  1.00 64.28
ATOM    934  N   PHE  127      51.902  41.189  27.274  1.00 64.96
ATOM    935  CA  PHE  127      51.177  39.948  27.565  1.00 65.21
ATOM    936  CB  PHE  127      50.145  39.657  26.468  1.00 64.22
ATOM    937  CG  PHE  127      49.569  38.258  26.525  1.00 63.67
ATOM    938  CD1 PHE  127      48.774  37.857  27.594  1.00 63.64
ATOM    939  CD2 PHE  127      49.830  37.343  25.512  1.00 63.42
```

Figure 4

```
ATOM    940  CE1 PHE   127      48.247  36.564  27.652  1.00 63.40
ATOM    941  CE2 PHE   127      49.308  36.051  25.560  1.00 63.55
ATOM    942  CZ  PHE   127      48.516  35.661  26.632  1.00 63.49
ATOM    943  C   PHE   127      52.154  38.791  27.631  1.00 65.83
ATOM    944  O   PHE   127      52.195  38.030  28.600  1.00 65.71
ATOM    945  N   LEU   128      52.931  38.684  26.562  1.00 66.57
ATOM    946  CA  LEU   128      53.942  37.656  26.387  1.00 67.52
ATOM    947  CB  LEU   128      54.773  38.022  25.166  1.00 67.64
ATOM    948  CG  LEU   128      53.926  38.452  23.969  1.00 67.42
ATOM    949  CD1 LEU   128      54.819  39.108  22.941  1.00 67.90
ATOM    950  CD2 LEU   128      53.195  37.251  23.387  1.00 67.65
ATOM    951  C   LEU   128      54.850  37.502  27.609  1.00 68.09
ATOM    952  O   LEU   128      54.829  36.468  28.285  1.00 67.92
ATOM    953  N   ASP   129      55.654  38.530  27.878  1.00 68.62
ATOM    954  CA  ASP   129      56.565  38.514  29.018  1.00 69.22
ATOM    955  CB  ASP   129      57.135  39.907  29.287  1.00 68.93
ATOM    956  CG  ASP   129      58.115  40.342  28.239  1.00 68.90
ATOM    957  OD1 ASP   129      59.100  39.606  28.011  1.00 69.12
ATOM    958  OD2 ASP   129      57.900  41.423  27.650  1.00 69.22
ATOM    959  C   ASP   129      55.843  38.059  30.267  1.00 69.59
ATOM    960  O   ASP   129      56.063  36.956  30.761  1.00 69.41
ATOM    961  N   LYS   130      54.973  38.940  30.753  1.00 70.10
ATOM    962  CA  LYS   130      54.190  38.733  31.958  1.00 70.67
ATOM    963  CB  LYS   130      53.285  39.946  32.159  1.00 70.80
ATOM    964  CG  LYS   130      54.076  41.252  32.052  1.00 70.54
ATOM    965  CD  LYS   130      53.218  42.479  32.266  1.00 70.22
ATOM    966  CE  LYS   130      54.021  43.746  32.011  1.00 70.07
ATOM    967  NZ  LYS   130      53.204  44.977  32.195  1.00 69.69
ATOM    968  C   LYS   130      53.394  37.441  31.982  1.00 71.17
ATOM    969  O   LYS   130      52.381  37.331  32.673  1.00 70.99
ATOM    970  N   HIS   131      53.883  36.468  31.221  1.00 72.01
ATOM    971  CA  HIS   131      53.301  35.139  31.125  1.00 73.44
ATOM    972  CB  HIS   131      52.313  35.065  29.965  1.00 73.00
ATOM    973  CG  HIS   131      50.881  35.076  30.397  1.00 72.93
ATOM    974  CD2 HIS   131      49.960  34.085  30.454  1.00 72.73
ATOM    975  ND1 HIS   131      50.256  36.210  30.869  1.00 72.87
ATOM    976  CE1 HIS   131      49.010  35.917  31.196  1.00 73.01
ATOM    977  NE2 HIS   131      48.806  34.634  30.954  1.00 73.04
ATOM    978  C   HIS   131      54.424  34.124  30.908  1.00 74.61
ATOM    979  O   HIS   131      54.419  33.049  31.514  1.00 74.70
ATOM    980  N   GLN   132      55.374  34.502  30.046  1.00 76.14
ATOM    981  CA  GLN   132      56.566  33.727  29.658  1.00 77.30
ATOM    982  CB  GLN   132      56.536  32.293  30.218  1.00 77.68
ATOM    983  CG  GLN   132      55.424  31.387  29.676  1.00 78.41
ATOM    984  CD  GLN   132      55.823  30.611  28.436  1.00 78.88
ATOM    985  OE1 GLN   132      56.016  31.179  27.356  1.00 78.50
ATOM    986  NE2 GLN   132      55.951  29.294  28.587  1.00 79.41
ATOM    987  C   GLN   132      56.673  33.682  28.134  1.00 77.86
ATOM    988  O   GLN   132      57.769  33.638  27.574  1.00 77.91
ATOM    989  N   MSE   133      55.520  33.703  27.472  1.00 78.39
ATOM    990  CA  MSE   133      55.450  33.662  26.017  1.00 78.88
ATOM    991  CB  MSE   133      53.989  33.684  25.551  1.00 80.96
ATOM    992  CG  MSE   133      53.278  32.347  25.586  1.00 83.34
ATOM    993  SE  MSE   133      51.991  32.273  26.846  1.00 87.09
ATOM    994  CE  MSE   133      52.168  30.521  27.421  1.00 84.33
ATOM    995  C   MSE   133      56.174  34.812  25.333  1.00 77.90
ATOM    996  O   MSE   133      55.552  35.548  24.567  1.00 78.34
ATOM    997  N   LYS   134      57.470  34.973  25.587  1.00 75.97
ATOM    998  CA  LYS   134      58.225  36.053  24.949  1.00 73.96
```

Figure 4

```
ATOM    999  CB  LYS   134      58.976  36.879  25.997  1.00 73.14
ATOM   1000  CG  LYS   134      59.676  38.125  25.454  1.00 72.28
ATOM   1001  CD  LYS   134      58.697  39.250  25.141  1.00 70.99
ATOM   1002  CE  LYS   134      59.415  40.586  24.935  1.00 70.06
ATOM   1003  NZ  LYS   134      60.234  40.640  23.687  1.00 69.46
ATOM   1004  C   LYS   134      59.211  35.443  23.964  1.00 72.94
ATOM   1005  O   LYS   134      59.727  36.123  23.077  1.00 72.63
ATOM   1006  N   HIS   135      59.457  34.148  24.132  1.00 72.28
ATOM   1007  CA  HIS   135      60.377  33.411  23.275  1.00 71.52
ATOM   1008  CB  HIS   135      61.359  32.584  24.119  1.00 71.15
ATOM   1009  CG  HIS   135      60.719  31.448  24.859  1.00 70.88
ATOM   1010  CD2 HIS   135      60.908  30.109  24.773  1.00 70.87
ATOM   1011  ND1 HIS   135      59.750  31.635  25.822  1.00 70.81
ATOM   1012  CE1 HIS   135      59.370  30.462  26.298  1.00 70.56
ATOM   1013  NE2 HIS   135      60.057  29.519  25.678  1.00 70.85
ATOM   1014  C   HIS   135      59.584  32.482  22.365  1.00 71.26
ATOM   1015  O   HIS   135      60.152  31.818  21.499  1.00 71.53
ATOM   1016  N   LYS   136      58.272  32.434  22.574  1.00 70.85
ATOM   1017  CA  LYS   136      57.393  31.590  21.766  1.00 70.33
ATOM   1018  CB  LYS   136      56.077  31.329  22.508  1.00 69.64
ATOM   1019  CG  LYS   136      56.225  30.694  23.886  1.00 68.45
ATOM   1020  CD  LYS   136      56.740  29.271  23.783  1.00 68.01
ATOM   1021  CE  LYS   136      56.698  28.560  25.128  1.00 67.56
ATOM   1022  NZ  LYS   136      55.303  28.356  25.623  1.00 66.87
ATOM   1023  C   LYS   136      57.088  32.296  20.443  1.00 70.46
ATOM   1024  O   LYS   136      57.100  33.530  20.371  1.00 70.94
ATOM   1025  N   LYS   137      56.828  31.519  19.396  1.00 70.16
ATOM   1026  CA  LYS   137      56.505  32.096  18.096  1.00 69.80
ATOM   1027  CB  LYS   137      57.505  31.642  17.023  1.00 71.09
ATOM   1028  CG  LYS   137      57.602  30.132  16.801  1.00 71.73
ATOM   1029  CD  LYS   137      58.567  29.840  15.654  1.00 72.44
ATOM   1030  CE  LYS   137      58.915  28.363  15.545  1.00 72.39
ATOM   1031  NZ  LYS   137      59.919  28.136  14.463  1.00 72.59
ATOM   1032  C   LYS   137      55.097  31.685  17.702  1.00 68.73
ATOM   1033  O   LYS   137      54.799  31.476  16.524  1.00 69.92
ATOM   1034  N   LEU   138      54.243  31.579  18.716  1.00 66.57
ATOM   1035  CA  LEU   138      52.841  31.193  18.586  1.00 63.82
ATOM   1036  CB  LEU   138      52.057  31.788  19.748  1.00 63.11
ATOM   1037  CG  LEU   138      52.364  31.145  21.092  1.00 62.89
ATOM   1038  CD1 LEU   138      51.924  32.068  22.220  1.00 62.68
ATOM   1039  CD2 LEU   138      51.669  29.786  21.150  1.00 61.80
ATOM   1040  C   LEU   138      52.114  31.553  17.294  1.00 62.26
ATOM   1041  O   LEU   138      52.416  32.566  16.647  1.00 62.54
ATOM   1042  N   PRO   139      51.149  30.708  16.894  1.00 60.11
ATOM   1043  CD  PRO   139      50.841  29.394  17.489  1.00 59.82
ATOM   1044  CA  PRO   139      50.356  30.937  15.682  1.00 57.91
ATOM   1045  CB  PRO   139      49.761  29.564  15.398  1.00 58.05
ATOM   1046  CG  PRO   139      49.573  28.999  16.772  1.00 59.12
ATOM   1047  C   PRO   139      49.302  31.968  16.101  1.00 55.89
ATOM   1048  O   PRO   139      48.469  31.693  16.973  1.00 55.71
ATOM   1049  N   LEU   140      49.358  33.154  15.501  1.00 53.40
ATOM   1050  CA  LEU   140      48.440  34.237  15.850  1.00 50.78
ATOM   1051  CB  LEU   140      49.195  35.576  15.834  1.00 49.87
ATOM   1052  CG  LEU   140      48.452  36.893  16.091  1.00 49.01
ATOM   1053  CD1 LEU   140      49.414  37.933  16.646  1.00 48.17
ATOM   1054  CD2 LEU   140      47.825  37.389  14.801  1.00 48.88
ATOM   1055  C   LEU   140      47.169  34.359  15.018  1.00 49.13
ATOM   1056  O   LEU   140      47.211  34.368  13.785  1.00 49.12
ATOM   1057  N   GLY   141      46.040  34.441  15.722  1.00 46.93
```

Figure 4

```
ATOM   1058  CA  GLY  141      44.743  34.613  15.086  1.00 43.70
ATOM   1059  C   GLY  141      44.324  36.041  15.402  1.00 41.11
ATOM   1060  O   GLY  141      44.277  36.414  16.569  1.00 41.46
ATOM   1061  N   PHE  142      44.018  36.842  14.388  1.00 38.27
ATOM   1062  CA  PHE  142      43.659  38.232  14.629  1.00 36.42
ATOM   1063  CB  PHE  142      44.648  39.118  13.882  1.00 34.58
ATOM   1064  CG  PHE  142      44.403  40.593  14.037  1.00 33.28
ATOM   1065  CD1 PHE  142      43.941  41.124  15.229  1.00 32.86
ATOM   1066  CD2 PHE  142      44.702  41.465  12.992  1.00 32.75
ATOM   1067  CE1 PHE  142      43.784  42.505  15.375  1.00 32.95
ATOM   1068  CE2 PHE  142      44.551  42.845  13.125  1.00 31.57
ATOM   1069  CZ  PHE  142      44.094  43.365  14.313  1.00 32.24
ATOM   1070  C   PHE  142      42.224  38.652  14.300  1.00 36.83
ATOM   1071  O   PHE  142      41.843  38.801  13.124  1.00 36.76
ATOM   1072  N   THR  143      41.423  38.848  15.347  1.00 35.96
ATOM   1073  CA  THR  143      40.047  39.288  15.156  1.00 34.35
ATOM   1074  CB  THR  143      39.179  38.997  16.373  1.00 33.98
ATOM   1075  OG1 THR  143      38.947  37.586  16.472  1.00 33.45
ATOM   1076  CG2 THR  143      37.854  39.750  16.255  1.00 33.35
ATOM   1077  C   THR  143      40.081  40.793  14.964  1.00 33.92
ATOM   1078  O   THR  143      40.190  41.544  15.928  1.00 34.30
ATOM   1079  N   PHE  144      40.009  41.227  13.716  1.00 33.00
ATOM   1080  CA  PHE  144      40.029  42.649  13.383  1.00 31.69
ATOM   1081  CB  PHE  144      40.891  42.842  12.132  1.00 29.18
ATOM   1082  CG  PHE  144      41.189  44.264  11.807  1.00 26.95
ATOM   1083  CD1 PHE  144      41.727  45.108  12.763  1.00 26.21
ATOM   1084  CD2 PHE  144      40.956  44.755  10.533  1.00 25.39
ATOM   1085  CE1 PHE  144      42.026  46.428  12.450  1.00 26.79
ATOM   1086  CE2 PHE  144      41.250  46.070  10.212  1.00 25.46
ATOM   1087  CZ  PHE  144      41.785  46.910  11.167  1.00 25.80
ATOM   1088  C   PHE  144      38.562  42.981  13.112  1.00 32.02
ATOM   1089  O   PHE  144      37.929  42.280  12.333  1.00 33.96
ATOM   1090  N   SER  145      38.025  44.027  13.744  1.00 32.29
ATOM   1091  CA  SER  145      36.602  44.387  13.600  1.00 31.56
ATOM   1092  CB  SER  145      35.993  44.689  14.968  1.00 31.79
ATOM   1093  OG  SER  145      35.997  43.539  15.790  1.00 33.15
ATOM   1094  C   SER  145      36.271  45.546  12.679  1.00 30.95
ATOM   1095  O   SER  145      35.601  46.508  13.082  1.00 30.63
ATOM   1096  N   PHE  146      36.723  45.456  11.439  1.00 30.27
ATOM   1097  CA  PHE  146      36.452  46.513  10.489  1.00 29.49
ATOM   1098  CB  PHE  146      37.573  47.541  10.535  1.00 29.01
ATOM   1099  CG  PHE  146      37.848  48.054  11.908  1.00 27.96
ATOM   1100  CD1 PHE  146      38.654  47.336  12.775  1.00 28.87
ATOM   1101  CD2 PHE  146      37.245  49.221  12.359  1.00 27.88
ATOM   1102  CE1 PHE  146      38.852  47.777  14.078  1.00 29.72
ATOM   1103  CE2 PHE  146      37.434  49.670  13.659  1.00 26.92
ATOM   1104  CZ  PHE  146      38.232  48.955  14.520  1.00 28.49
ATOM   1105  C   PHE  146      36.318  45.937   9.093  1.00 29.49
ATOM   1106  O   PHE  146      36.668  44.778   8.846  1.00 29.56
ATOM   1107  N   PRO  147      35.805  46.738   8.152  1.00 29.02
ATOM   1108  CD  PRO  147      35.452  48.167   8.211  1.00 28.09
ATOM   1109  CA  PRO  147      35.662  46.212   6.798  1.00 30.12
ATOM   1110  CB  PRO  147      34.852  47.309   6.099  1.00 28.65
ATOM   1111  CG  PRO  147      35.377  48.540   6.749  1.00 28.13
ATOM   1112  C   PRO  147      37.047  45.969   6.179  1.00 30.89
ATOM   1113  O   PRO  147      37.938  46.821   6.263  1.00 32.17
ATOM   1114  N   VAL  148      37.221  44.807   5.557  1.00 31.62
ATOM   1115  CA  VAL  148      38.499  44.453   4.957  1.00 32.00
ATOM   1116  CB  VAL  148      39.399  43.733   6.002  1.00 32.44
```

Figure 4

```
ATOM   1117  CG1 VAL   148      40.471  42.940   5.311  1.00 33.36
ATOM   1118  CG2 VAL   148      40.035  44.758   6.934  1.00 32.04
ATOM   1119  C   VAL   148      38.351  43.557   3.733  1.00 31.54
ATOM   1120  O   VAL   148      37.937  42.402   3.858  1.00 30.91
ATOM   1121  N   ALA   149      38.688  44.091   2.560  1.00 31.66
ATOM   1122  CA  ALA   149      38.610  43.316   1.324  1.00 32.33
ATOM   1123  CB  ALA   149      38.834  44.213   0.120  1.00 31.16
ATOM   1124  C   ALA   149      39.723  42.288   1.428  1.00 33.43
ATOM   1125  O   ALA   149      40.882  42.653   1.431  1.00 35.59
ATOM   1126  N   HIS   150      39.387  41.008   1.535  1.00 33.73
ATOM   1127  CA  HIS   150      40.410  39.980   1.666  1.00 33.88
ATOM   1128  CB  HIS   150      39.868  38.780   2.450  1.00 34.82
ATOM   1129  CG  HIS   150      39.879  38.961   3.933  1.00 35.58
ATOM   1130  CD2 HIS   150      40.344  38.162   4.921  1.00 36.49
ATOM   1131  ND1 HIS   150      39.329  40.061   4.555  1.00 36.45
ATOM   1132  CE1 HIS   150      39.454  39.930   5.865  1.00 36.79
ATOM   1133  NE2 HIS   150      40.067  38.786   6.114  1.00 36.38
ATOM   1134  C   HIS   150      40.960  39.442   0.353  1.00 34.39
ATOM   1135  O   HIS   150      40.245  39.364  -0.655  1.00 34.56
ATOM   1136  N   ALA   151      42.239  39.068   0.380  1.00 34.73
ATOM   1137  CA  ALA   151      42.898  38.440  -0.762  1.00 34.53
ATOM   1138  CB  ALA   151      44.334  38.949  -0.919  1.00 34.86
ATOM   1139  C   ALA   151      42.894  36.968  -0.338  1.00 34.46
ATOM   1140  O   ALA   151      42.734  36.065  -1.161  1.00 34.16
ATOM   1141  N   ASP   152      43.050  36.754   0.970  1.00 34.36
ATOM   1142  CA  ASP   152      43.045  35.422   1.562  1.00 35.45
ATOM   1143  CB  ASP   152      44.335  34.687   1.214  1.00 37.69
ATOM   1144  CG  ASP   152      44.233  33.185   1.431  1.00 40.20
ATOM   1145  OD1 ASP   152      43.219  32.717   2.007  1.00 40.73
ATOM   1146  OD2 ASP   152      45.177  32.464   1.018  1.00 42.29
ATOM   1147  C   ASP   152      42.901  35.549   3.088  1.00 35.53
ATOM   1148  O   ASP   152      43.048  36.642   3.642  1.00 35.08
ATOM   1149  N   ILE   153      42.627  34.433   3.762  1.00 35.49
ATOM   1150  CA  ILE   153      42.436  34.427   5.213  1.00 35.75
ATOM   1151  CB  ILE   153      42.258  32.984   5.754  1.00 35.32
ATOM   1152  CG2 ILE   153      43.609  32.316   5.937  1.00 34.16
ATOM   1153  CG1 ILE   153      41.593  33.022   7.130  1.00 35.44
ATOM   1154  CD1 ILE   153      40.225  33.697   7.131  1.00 36.43
ATOM   1155  C   ILE   153      43.571  35.079   6.011  1.00 36.77
ATOM   1156  O   ILE   153      43.450  35.278   7.229  1.00 36.40
ATOM   1157  N   ASP   154      44.665  35.411   5.332  1.00 37.10
ATOM   1158  CA  ASP   154      45.815  36.003   6.000  1.00 37.27
ATOM   1159  CB  ASP   154      46.982  35.013   5.991  1.00 38.98
ATOM   1160  CG  ASP   154      47.795  35.079   4.703  1.00 41.58
ATOM   1161  OD1 ASP   154      47.215  34.890   3.605  1.00 42.46
ATOM   1162  OD2 ASP   154      49.022  35.331   4.789  1.00 42.65
ATOM   1163  C   ASP   154      46.233  37.287   5.307  1.00 36.74
ATOM   1164  O   ASP   154      47.360  37.751   5.471  1.00 37.07
ATOM   1165  N   ALA   155      45.328  37.865   4.531  1.00 35.91
ATOM   1166  CA  ALA   155      45.650  39.093   3.830  1.00 36.20
ATOM   1167  CB  ALA   155      46.522  38.771   2.621  1.00 36.22
ATOM   1168  C   ALA   155      44.412  39.864   3.387  1.00 36.20
ATOM   1169  O   ALA   155      43.490  39.289   2.820  1.00 36.87
ATOM   1170  N   GLY   156      44.402  41.168   3.642  1.00 36.26
ATOM   1171  CA  GLY   156      43.279  41.997   3.245  1.00 37.08
ATOM   1172  C   GLY   156      43.481  43.446   3.647  1.00 38.10
ATOM   1173  O   GLY   156      44.027  43.727   4.711  1.00 38.52
ATOM   1174  N   ILE   157      43.052  44.377   2.805  1.00 39.16
ATOM   1175  CA  ILE   157      43.203  45.789   3.125  1.00 41.42
```

```
ATOM   1176  CB  ILE  157      43.389  46.646   1.842  1.00 42.84
ATOM   1177  CG2 ILE  157      44.844  46.550   1.349  1.00 44.32
ATOM   1178  CG1 ILE  157      42.399  46.193   0.761  1.00 43.93
ATOM   1179  CD1 ILE  157      42.630  46.838  -0.615  1.00 44.55
ATOM   1180  C   ILE  157      42.010  46.331   3.921  1.00 42.26
ATOM   1181  O   ILE  157      40.864  45.912   3.732  1.00 42.28
ATOM   1182  N   LEU  158      42.300  47.259   4.824  1.00 42.54
ATOM   1183  CA  LEU  158      41.283  47.873   5.648  1.00 43.22
ATOM   1184  CB  LEU  158      41.928  48.504   6.884  1.00 44.12
ATOM   1185  CG  LEU  158      41.090  49.514   7.670  1.00 44.84
ATOM   1186  CD1 LEU  158      40.020  48.782   8.472  1.00 45.23
ATOM   1187  CD2 LEU  158      42.006  50.320   8.590  1.00 45.09
ATOM   1188  C   LEU  158      40.548  48.947   4.855  1.00 43.56
ATOM   1189  O   LEU  158      40.984  50.099   4.801  1.00 43.77
ATOM   1190  N   LEU  159      39.434  48.569   4.239  1.00 43.40
ATOM   1191  CA  LEU  159      38.634  49.508   3.465  1.00 43.01
ATOM   1192  CB  LEU  159      37.238  48.935   3.280  1.00 43.36
ATOM   1193  CG  LEU  159      37.279  47.599   2.539  1.00 43.44
ATOM   1194  CD1 LEU  159      36.020  46.808   2.829  1.00 44.00
ATOM   1195  CD2 LEU  159      37.443  47.857   1.050  1.00 42.93
ATOM   1196  C   LEU  159      38.564  50.879   4.139  1.00 42.62
ATOM   1197  O   LEU  159      38.745  51.905   3.488  1.00 43.03
ATOM   1198  N   ASN  160      38.297  50.902   5.440  1.00 42.20
ATOM   1199  CA  ASN  160      38.243  52.169   6.170  1.00 41.99
ATOM   1200  CB  ASN  160      37.347  53.197   5.447  1.00 42.23
ATOM   1201  CG  ASN  160      35.913  52.733   5.295  1.00 43.38
ATOM   1202  OD1 ASN  160      35.225  53.102   4.334  1.00 42.38
ATOM   1203  ND2 ASN  160      35.444  51.934   6.250  1.00 44.48
ATOM   1204  C   ASN  160      37.813  51.988   7.616  1.00 41.13
ATOM   1205  O   ASN  160      37.359  50.913   8.011  1.00 41.17
ATOM   1206  N   TRP  161      37.980  53.043   8.403  1.00 40.24
ATOM   1207  CA  TRP  161      37.652  53.004   9.824  1.00 39.69
ATOM   1208  CB  TRP  161      38.522  54.003  10.602  1.00 39.33
ATOM   1209  CG  TRP  161      39.987  53.640  10.769  1.00 39.07
ATOM   1210  CD2 TRP  161      40.527  52.469  11.411  1.00 38.63
ATOM   1211  CE2 TRP  161      41.931  52.616  11.438  1.00 38.27
ATOM   1212  CE3 TRP  161      39.960  51.317  11.972  1.00 38.43
ATOM   1213  CD1 TRP  161      41.060  54.417  10.436  1.00 38.40
ATOM   1214  NE1 TRP  161      42.228  53.812  10.840  1.00 38.42
ATOM   1215  CZ2 TRP  161      42.778  51.659  12.000  1.00 38.26
ATOM   1216  CZ3 TRP  161      40.809  50.357  12.538  1.00 38.07
ATOM   1217  CH2 TRP  161      42.200  50.540  12.545  1.00 38.37
ATOM   1218  C   TRP  161      36.196  53.301  10.150  1.00 39.07
ATOM   1219  O   TRP  161      35.578  54.193   9.562  1.00 39.38
ATOM   1220  N   THR  162      35.668  52.555  11.114  1.00 38.45
ATOM   1221  CA  THR  162      34.302  52.734  11.593  1.00 38.37
ATOM   1222  CB  THR  162      33.381  51.600  11.125  1.00 37.71
ATOM   1223  OG1 THR  162      33.926  50.338  11.548  1.00 37.02
ATOM   1224  CG2 THR  162      33.226  51.635   9.617  1.00 36.52
ATOM   1225  C   THR  162      34.357  52.702  13.121  1.00 38.24
ATOM   1226  O   THR  162      35.405  52.443  13.703  1.00 37.86
ATOM   1227  N   LYS  163      33.231  52.968  13.770  1.00 38.99
ATOM   1228  CA  LYS  163      33.192  52.941  15.222  1.00 39.72
ATOM   1229  CB  LYS  163      33.510  51.528  15.728  1.00 38.16
ATOM   1230  CG  LYS  163      32.467  50.487  15.311  1.00 36.62
ATOM   1231  CD  LYS  163      32.727  49.108  15.918  1.00 34.66
ATOM   1232  CE  LYS  163      33.829  48.349  15.195  1.00 33.22
ATOM   1233  NZ  LYS  163      34.068  47.031  15.850  1.00 32.19
ATOM   1234  C   LYS  163      34.142  53.956  15.848  1.00 40.71
```

```
ATOM   1235  O   LYS  163      34.690  53.723  16.931  1.00 40.69
ATOM   1236  N   GLY  164      34.338  55.076  15.156  1.00 41.81
ATOM   1237  CA  GLY  164      35.187  56.139  15.672  1.00 43.90
ATOM   1238  C   GLY  164      36.685  56.031  15.463  1.00 45.41
ATOM   1239  O   GLY  164      37.375  57.055  15.381  1.00 45.25
ATOM   1240  N   PHE  165      37.190  54.802  15.397  1.00 47.06
ATOM   1241  CA  PHE  165      38.613  54.560  15.197  1.00 48.70
ATOM   1242  CB  PHE  165      38.852  53.117  14.767  1.00 47.20
ATOM   1243  CG  PHE  165      39.290  52.222  15.870  1.00 45.64
ATOM   1244  CD1 PHE  165      38.443  51.937  16.929  1.00 45.87
ATOM   1245  CD2 PHE  165      40.544  51.632  15.833  1.00 45.19
ATOM   1246  CE1 PHE  165      38.840  51.064  17.945  1.00 46.28
ATOM   1247  CE2 PHE  165      40.952  50.763  16.834  1.00 45.80
ATOM   1248  CZ  PHE  165      40.098  50.475  17.896  1.00 45.96
ATOM   1249  C   PHE  165      39.250  55.471  14.154  1.00 50.94
ATOM   1250  O   PHE  165      38.633  55.823  13.143  1.00 50.36
ATOM   1251  N   LYS  166      40.500  55.838  14.415  1.00 53.77
ATOM   1252  CA  LYS  166      41.275  56.680  13.514  1.00 56.56
ATOM   1253  CB  LYS  166      41.050  58.170  13.822  1.00 56.16
ATOM   1254  CG  LYS  166      39.720  58.697  13.290  1.00 56.44
ATOM   1255  CD  LYS  166      39.524  58.320  11.812  1.00 56.54
ATOM   1256  CE  LYS  166      38.131  58.694  11.305  1.00 56.74
ATOM   1257  NZ  LYS  166      37.863  58.198   9.922  1.00 56.86
ATOM   1258  C   LYS  166      42.751  56.322  13.640  1.00 58.33
ATOM   1259  O   LYS  166      43.180  55.747  14.651  1.00 58.69
ATOM   1260  N   ALA  167      43.510  56.647  12.597  1.00 59.76
ATOM   1261  CA  ALA  167      44.943  56.375  12.543  1.00 61.43
ATOM   1262  CB  ALA  167      45.220  54.901  12.834  1.00 60.92
ATOM   1263  C   ALA  167      45.401  56.725  11.137  1.00 62.76
ATOM   1264  O   ALA  167      45.147  55.967  10.197  1.00 63.38
ATOM   1265  N   SER  168      46.066  57.872  10.999  1.00 63.98
ATOM   1266  CA  SER  168      46.556  58.345   9.704  1.00 64.43
ATOM   1267  CB  SER  168      47.636  59.414   9.903  1.00 64.96
ATOM   1268  OG  SER  168      47.130  60.546  10.594  1.00 65.76
ATOM   1269  C   SER  168      47.115  57.216   8.846  1.00 64.59
ATOM   1270  O   SER  168      47.805  56.322   9.347  1.00 64.35
ATOM   1271  N   GLY  169      46.800  57.260   7.553  1.00 64.75
ATOM   1272  CA  GLY  169      47.280  56.245   6.632  1.00 65.55
ATOM   1273  C   GLY  169      47.158  54.821   7.142  1.00 65.88
ATOM   1274  O   GLY  169      48.151  54.097   7.255  1.00 65.72
ATOM   1275  N   ALA  170      45.936  54.416   7.465  1.00 66.32
ATOM   1276  CA  ALA  170      45.699  53.065   7.947  1.00 66.82
ATOM   1277  CB  ALA  170      44.930  53.100   9.256  1.00 66.65
ATOM   1278  C   ALA  170      44.890  52.346   6.879  1.00 67.02
ATOM   1279  O   ALA  170      45.209  51.226   6.477  1.00 67.31
ATOM   1280  N   GLU  171      43.847  53.017   6.410  1.00 66.85
ATOM   1281  CA  GLU  171      42.979  52.463   5.387  1.00 66.80
ATOM   1282  CB  GLU  171      41.705  53.292   5.287  1.00 67.90
ATOM   1283  CG  GLU  171      41.958  54.783   5.279  1.00 69.27
ATOM   1284  CD  GLU  171      40.850  55.552   4.590  1.00 70.17
ATOM   1285  OE1 GLU  171      40.789  55.506   3.340  1.00 70.45
ATOM   1286  OE2 GLU  171      40.038  56.191   5.296  1.00 70.67
ATOM   1287  C   GLU  171      43.666  52.427   4.032  1.00 65.92
ATOM   1288  O   GLU  171      44.469  53.301   3.711  1.00 66.22
ATOM   1289  N   GLY  172      43.339  51.408   3.242  1.00 64.69
ATOM   1290  CA  GLY  172      43.922  51.265   1.925  1.00 62.79
ATOM   1291  C   GLY  172      45.096  50.312   1.882  1.00 61.61
ATOM   1292  O   GLY  172      45.493  49.884   0.805  1.00 61.59
ATOM   1293  N   ASN  173      45.643  49.965   3.045  1.00 60.93
```

Figure 4

	ATOM	1294	CA	ASN	173	46.800	49.065	3.115	1.00	60.42
	ATOM	1295	CB	ASN	173	47.922	49.722	3.913	1.00	61.72
	ATOM	1296	CG	ASN	173	48.035	51.201	3.631	1.00	62.78
	ATOM	1297	OD1	ASN	173	48.367	51.605	2.515	1.00	63.29
5	ATOM	1298	ND2	ASN	173	47.741	52.024	4.637	1.00	63.06
	ATOM	1299	C	ASN	173	46.463	47.747	3.771	1.00	59.26
	ATOM	1300	O	ASN	173	45.440	47.624	4.430	1.00	59.57
	ATOM	1301	N	ASN	174	47.336	46.763	3.598	1.00	58.79
	ATOM	1302	CA	ASN	174	47.126	45.447	4.196	1.00	58.46
10	ATOM	1303	CB	ASN	174	48.264	44.495	3.793	1.00	57.45
	ATOM	1304	CG	ASN	174	48.104	43.093	4.375	1.00	57.22
	ATOM	1305	OD1	ASN	174	48.757	42.144	3.924	1.00	56.21
	ATOM	1306	ND2	ASN	174	47.245	42.957	5.382	1.00	56.76
	ATOM	1307	C	ASN	174	47.083	45.615	5.712	1.00	58.42
15	ATOM	1308	O	ASN	174	47.927	46.302	6.281	1.00	59.03
	ATOM	1309	N	VAL	175	46.091	45.008	6.359	1.00	58.23
	ATOM	1310	CA	VAL	175	45.966	45.106	7.809	1.00	57.79
	ATOM	1311	CB	VAL	175	44.544	44.765	8.295	1.00	57.69
	ATOM	1312	CG1	VAL	175	44.461	44.933	9.807	1.00	56.81
20	ATOM	1313	CG2	VAL	175	43.531	45.665	7.603	1.00	57.69
	ATOM	1314	C	VAL	175	46.944	44.150	8.470	1.00	57.62
	ATOM	1315	O	VAL	175	47.734	44.560	9.319	1.00	57.89
	ATOM	1316	N	VAL	176	46.896	42.878	8.086	1.00	57.24
	ATOM	1317	CA	VAL	176	47.818	41.904	8.660	1.00	57.25
25	ATOM	1318	CB	VAL	176	47.638	40.501	8.037	1.00	57.27
	ATOM	1319	CG1	VAL	176	48.597	39.511	8.701	1.00	56.21
	ATOM	1320	CG2	VAL	176	46.196	40.035	8.199	1.00	56.28
	ATOM	1321	C	VAL	176	49.232	42.396	8.362	1.00	57.38
	ATOM	1322	O	VAL	176	50.212	41.911	8.926	1.00	57.30
30	ATOM	1323	N	GLY	177	49.319	43.374	7.467	1.00	57.41
	ATOM	1324	CA	GLY	177	50.605	43.939	7.103	1.00	57.60
	ATOM	1325	C	GLY	177	51.135	44.878	8.170	1.00	57.50
	ATOM	1326	O	GLY	177	52.171	44.605	8.781	1.00	58.09
	ATOM	1327	N	LEU	178	50.425	45.982	8.396	1.00	56.68
35	ATOM	1328	CA	LEU	178	50.837	46.959	9.396	1.00	55.42
	ATOM	1329	CB	LEU	178	49.710	47.968	9.646	1.00	55.02
	ATOM	1330	CG	LEU	178	49.394	48.906	8.466	1.00	54.15
	ATOM	1331	CD1	LEU	178	48.158	49.743	8.766	1.00	53.80
	ATOM	1332	CD2	LEU	178	50.588	49.815	8.197	1.00	54.17
40	ATOM	1333	C	LEU	178	51.247	46.279	10.701	1.00	54.84
	ATOM	1334	O	LEU	178	52.177	46.717	11.375	1.00	55.07
	ATOM	1335	N	LEU	179	50.575	45.192	11.050	1.00	53.85
	ATOM	1336	CA	LEU	179	50.917	44.491	12.274	1.00	53.57
	ATOM	1337	CB	LEU	179	49.882	43.409	12.582	1.00	52.75
45	ATOM	1338	CG	LEU	179	50.099	42.671	13.907	1.00	52.23
	ATOM	1339	CD1	LEU	179	49.689	43.580	15.056	1.00	51.63
	ATOM	1340	CD2	LEU	179	49.286	41.381	13.935	1.00	51.34
	ATOM	1341	C	LEU	179	52.286	43.845	12.128	1.00	54.26
	ATOM	1342	O	LEU	179	53.070	43.796	13.075	1.00	54.60
50	ATOM	1343	N	ARG	180	52.576	43.343	10.932	1.00	54.59
	ATOM	1344	CA	ARG	180	53.855	42.679	10.688	1.00	54.08
	ATOM	1345	CB	ARG	180	53.824	41.911	9.357	1.00	52.59
	ATOM	1346	CG	ARG	180	53.273	40.498	9.515	1.00	50.37
	ATOM	1347	CD	ARG	180	53.276	39.702	8.223	1.00	47.24
55	ATOM	1348	NE	ARG	180	52.610	38.420	8.425	1.00	45.06
	ATOM	1349	CZ	ARG	180	51.979	37.754	7.462	1.00	43.97
	ATOM	1350	NH1	ARG	180	51.935	38.256	6.226	1.00	42.53
	ATOM	1351	NH2	ARG	180	51.366	36.601	7.735	1.00	42.95
	ATOM	1352	C	ARG	180	55.059	43.605	10.732	1.00	54.76

Figure 4

```
ATOM   1353  O   ARG  180      56.009  43.343  11.473  1.00 54.65
ATOM   1354  N   ASP  181      55.036  44.681   9.951  1.00 55.34
ATOM   1355  CA  ASP  181      56.169  45.593   9.972  1.00 56.60
ATOM   1356  CB  ASP  181      56.266  46.386   8.649  1.00 56.43
ATOM   1357  CG  ASP  181      55.132  47.382   8.448  1.00 55.64
ATOM   1358  OD1 ASP  181      54.658  47.483   7.294  1.00 55.20
ATOM   1359  OD2 ASP  181      54.734  48.076   9.416  1.00 55.23
ATOM   1360  C   ASP  181      56.115  46.514  11.199  1.00 57.64
ATOM   1361  O   ASP  181      56.510  47.685  11.153  1.00 57.96
ATOM   1362  N   ALA  182      55.634  45.947  12.303  1.00 57.87
ATOM   1363  CA  ALA  182      55.524  46.646  13.577  1.00 57.84
ATOM   1364  CB  ALA  182      54.078  47.048  13.836  1.00 58.19
ATOM   1365  C   ALA  182      56.013  45.683  14.657  1.00 57.83
ATOM   1366  O   ALA  182      56.681  46.094  15.611  1.00 58.32
ATOM   1367  N   ILE  183      55.669  44.404  14.505  1.00 57.35
ATOM   1368  CA  ILE  183      56.109  43.381  15.448  1.00 57.40
ATOM   1369  CB  ILE  183      55.374  42.036  15.233  1.00 56.09
ATOM   1370  CG2 ILE  183      56.025  40.932  16.074  1.00 55.25
ATOM   1371  CG1 ILE  183      53.904  42.174  15.628  1.00 55.30
ATOM   1372  CD1 ILE  183      53.115  40.881  15.505  1.00 54.14
ATOM   1373  C   ILE  183      57.600  43.164  15.199  1.00 58.51
ATOM   1374  O   ILE  183      58.294  42.531  16.002  1.00 59.24
ATOM   1375  N   LYS  184      58.093  43.689  14.077  1.00 59.04
ATOM   1376  CA  LYS  184      59.508  43.550  13.757  1.00 59.19
ATOM   1377  CB  LYS  184      59.719  43.243  12.268  1.00 59.15
ATOM   1378  CG  LYS  184      59.356  44.354  11.310  1.00 58.36
ATOM   1379  CD  LYS  184      59.566  43.897   9.868  1.00 58.59
ATOM   1380  CE  LYS  184      58.637  42.735   9.500  1.00 59.26
ATOM   1381  NZ  LYS  184      58.751  42.306   8.067  1.00 59.63
ATOM   1382  C   LYS  184      60.270  44.806  14.155  1.00 59.27
ATOM   1383  O   LYS  184      61.382  44.705  14.667  1.00 59.28
ATOM   1384  N   ARG  185      59.695  45.984  13.923  1.00 59.21
ATOM   1385  CA  ARG  185      60.383  47.211  14.331  1.00 59.69
ATOM   1386  CB  ARG  185      59.545  48.458  14.060  1.00 59.70
ATOM   1387  CG  ARG  185      59.278  48.772  12.610  1.00 60.85
ATOM   1388  CD  ARG  185      59.138  50.280  12.443  1.00 60.89
ATOM   1389  NE  ARG  185      58.121  50.628  11.459  1.00 62.26
ATOM   1390  CZ  ARG  185      56.819  50.403  11.620  1.00 61.84
ATOM   1391  NH1 ARG  185      56.372  49.828  12.731  1.00 61.22
ATOM   1392  NH2 ARG  185      55.966  50.754  10.666  1.00 62.23
ATOM   1393  C   ARG  185      60.574  47.104  15.836  1.00 60.41
ATOM   1394  O   ARG  185      61.630  47.430  16.384  1.00 60.45
ATOM   1395  N   ARG  186      59.518  46.633  16.489  1.00 61.07
ATOM   1396  CA  ARG  186      59.489  46.460  17.933  1.00 61.42
ATOM   1397  CB  ARG  186      58.066  46.055  18.358  1.00 61.16
ATOM   1398  CG  ARG  186      57.666  46.433  19.786  1.00 61.08
ATOM   1399  CD  ARG  186      58.249  45.473  20.828  1.00 60.87
ATOM   1400  NE  ARG  186      57.917  45.894  22.188  1.00 61.44
ATOM   1401  CZ  ARG  186      58.294  45.246  23.288  1.00 60.67
ATOM   1402  NH1 ARG  186      59.024  44.133  23.201  1.00 60.28
ATOM   1403  NH2 ARG  186      57.942  45.712  24.481  1.00 61.46
ATOM   1404  C   ARG  186      60.516  45.399  18.344  1.00 61.85
ATOM   1405  O   ARG  186      60.980  44.610  17.514  1.00 62.16
ATOM   1406  N   GLY  187      60.873  45.401  19.628  1.00 62.07
ATOM   1407  CA  GLY  187      61.843  44.455  20.157  1.00 62.22
ATOM   1408  C   GLY  187      61.591  43.017  19.754  1.00 62.50
ATOM   1409  O   GLY  187      60.541  42.692  19.202  1.00 62.37
ATOM   1410  N   ASP  188      62.556  42.148  20.036  1.00 63.08
ATOM   1411  CA  ASP  188      62.414  40.746  19.684  1.00 62.67
```

```
ATOM   1412  CB  ASP   188      63.465  39.873  20.373  1.00 61.80
ATOM   1413  CG  ASP   188      63.027  38.409  20.468  1.00 60.64
ATOM   1414  OD1 ASP   188      62.125  38.107  21.289  1.00 60.77
ATOM   1415  OD2 ASP   188      63.565  37.563  19.715  1.00 60.43
ATOM   1416  C   ASP   188      61.047  40.193  20.022  1.00 63.58
ATOM   1417  O   ASP   188      60.441  40.539  21.044  1.00 62.69
ATOM   1418  N   PHE   189      60.599  39.309  19.138  1.00 64.49
ATOM   1419  CA  PHE   189      59.327  38.632  19.249  1.00 64.75
ATOM   1420  CB  PHE   189      58.233  39.629  19.598  1.00 64.84
ATOM   1421  CG  PHE   189      56.886  39.010  19.689  1.00 65.46
ATOM   1422  CD1 PHE   189      56.707  37.824  20.402  1.00 65.54
ATOM   1423  CD2 PHE   189      55.795  39.592  19.052  1.00 65.28
ATOM   1424  CE1 PHE   189      55.455  37.224  20.481  1.00 65.61
ATOM   1425  CE2 PHE   189      54.542  39.007  19.122  1.00 65.71
ATOM   1426  CZ  PHE   189      54.369  37.819  19.839  1.00 65.57
ATOM   1427  C   PHE   189      59.018  37.952  17.919  1.00 65.33
ATOM   1428  O   PHE   189      58.921  38.609  16.881  1.00 64.91
ATOM   1429  N   GLU   190      58.879  36.631  17.956  1.00 66.13
ATOM   1430  CA  GLU   190      58.584  35.854  16.752  1.00 66.57
ATOM   1431  CB  GLU   190      59.387  34.545  16.755  1.00 66.34
ATOM   1432  CG  GLU   190      60.778  34.649  17.389  1.00 64.66
ATOM   1433  CD  GLU   190      61.908  34.356  16.411  1.00 64.02
ATOM   1434  OE1 GLU   190      63.054  34.161  16.874  1.00 63.09
ATOM   1435  OE2 GLU   190      61.658  34.327  15.186  1.00 63.04
ATOM   1436  C   GLU   190      57.093  35.528  16.745  1.00 67.09
ATOM   1437  O   GLU   190      56.609  34.828  17.638  1.00 67.36
ATOM   1438  N   MSE   191      56.367  36.030  15.747  1.00 67.05
ATOM   1439  CA  MSE   191      54.928  35.775  15.666  1.00 66.65
ATOM   1440  CB  MSE   191      54.164  36.920  16.347  1.00 69.47
ATOM   1441  CG  MSE   191      52.867  36.492  17.037  1.00 72.30
ATOM   1442  SE  MSE   191      53.120  35.293  18.409  1.00 78.56
ATOM   1443  CE  MSE   191      51.941  35.893  19.581  1.00 75.88
ATOM   1444  C   MSE   191      54.412  35.590  14.230  1.00 64.85
ATOM   1445  O   MSE   191      54.399  36.538  13.435  1.00 64.30
ATOM   1446  N   ASP   192      53.977  34.368  13.910  1.00 62.82
ATOM   1447  CA  ASP   192      53.449  34.051  12.580  1.00 60.76
ATOM   1448  CB  ASP   192      53.774  32.607  12.207  1.00 61.24
ATOM   1449  CG  ASP   192      55.210  32.427  11.792  1.00 61.76
ATOM   1450  OD1 ASP   192      55.684  33.219  10.947  1.00 62.45
ATOM   1451  OD2 ASP   192      55.863  31.492  12.299  1.00 62.32
ATOM   1452  C   ASP   192      51.942  34.266  12.459  1.00 59.03
ATOM   1453  O   ASP   192      51.143  33.375  12.767  1.00 58.37
ATOM   1454  N   VAL   193      51.567  35.453  11.991  1.00 57.00
ATOM   1455  CA  VAL   193      50.167  35.818  11.818  1.00 54.85
ATOM   1456  CB  VAL   193      50.034  37.305  11.454  1.00 55.09
ATOM   1457  CG1 VAL   193      48.568  37.712  11.448  1.00 54.84
ATOM   1458  CG2 VAL   193      50.826  38.146  12.441  1.00 54.87
ATOM   1459  C   VAL   193      49.473  34.977  10.746  1.00 53.19
ATOM   1460  O   VAL   193      49.500  35.303   9.555  1.00 52.03
ATOM   1461  N   VAL   194      48.854  33.894  11.205  1.00 51.82
ATOM   1462  CA  VAL   194      48.126  32.949  10.367  1.00 50.66
ATOM   1463  CB  VAL   194      47.841  31.644  11.174  1.00 51.08
ATOM   1464  CG1 VAL   194      46.686  30.860  10.554  1.00 52.09
ATOM   1465  CG2 VAL   194      49.091  30.778  11.211  1.00 51.33
ATOM   1466  C   VAL   194      46.798  33.498   9.808  1.00 49.99
ATOM   1467  O   VAL   194      46.677  33.726   8.602  1.00 49.40
ATOM   1468  N   ALA   195      45.813  33.723  10.683  1.00 48.93
ATOM   1469  CA  ALA   195      44.499  34.193  10.251  1.00 47.60
ATOM   1470  CB  ALA   195      43.467  33.123  10.572  1.00 47.58
```

Figure 4

```
ATOM   1471  C   ALA  195      43.992  35.546  10.760  1.00 46.68
ATOM   1472  O   ALA  195      44.344  35.996  11.851  1.00 46.16
ATOM   1473  N   MSE  196      43.157  36.182   9.940  1.00 45.43
ATOM   1474  CA  MSE  196      42.521  37.459  10.279  1.00 44.60
ATOM   1475  CB  MSE  196      43.079  38.623   9.451  1.00 45.32
ATOM   1476  CG  MSE  196      42.329  39.925   9.716  1.00 47.29
ATOM   1477  SE  MSE  196      42.937  41.426   8.852  1.00 53.21
ATOM   1478  CE  MSE  196      44.264  41.920   9.982  1.00 51.44
ATOM   1479  C   MSE  196      41.019  37.333  10.002  1.00 43.09
ATOM   1480  O   MSE  196      40.610  36.973   8.892  1.00 43.71
ATOM   1481  N   VAL  197      40.190  37.631  10.996  1.00 40.47
ATOM   1482  CA  VAL  197      38.751  37.514  10.799  1.00 37.00
ATOM   1483  CB  VAL  197      38.240  36.228  11.458  1.00 37.31
ATOM   1484  CG1 VAL  197      38.840  35.004  10.766  1.00 36.64
ATOM   1485  CG2 VAL  197      38.643  36.217  12.914  1.00 36.88
ATOM   1486  C   VAL  197      37.991  38.710  11.354  1.00 35.22
ATOM   1487  O   VAL  197      38.561  39.544  12.057  1.00 35.21
ATOM   1488  N   ASN  198      36.708  38.801  11.015  1.00 33.39
ATOM   1489  CA  ASN  198      35.830  39.883  11.491  1.00 30.23
ATOM   1490  CB  ASN  198      34.740  40.175  10.446  1.00 30.65
ATOM   1491  CG  ASN  198      33.801  41.309  10.852  1.00 31.35
ATOM   1492  OD1 ASN  198      32.907  41.128  11.686  1.00 32.70
ATOM   1493  ND2 ASN  198      33.997  42.486  10.251  1.00 30.53
ATOM   1494  C   ASN  198      35.217  39.356  12.780  1.00 28.41
ATOM   1495  O   ASN  198      35.052  38.143  12.937  1.00 26.14
ATOM   1496  N   ASP  199      34.892  40.252  13.711  1.00 27.77
ATOM   1497  CA  ASP  199      34.325  39.816  14.990  1.00 26.87
ATOM   1498  CB  ASP  199      34.156  41.007  15.945  1.00 26.75
ATOM   1499  CG  ASP  199      33.254  42.097  15.396  1.00 26.24
ATOM   1500  OD1 ASP  199      33.221  42.292  14.167  1.00 26.90
ATOM   1501  OD2 ASP  199      32.587  42.777  16.205  1.00 26.19
ATOM   1502  C   ASP  199      33.027  39.034  14.843  1.00 26.43
ATOM   1503  O   ASP  199      32.715  38.188  15.684  1.00 27.02
ATOM   1504  N   THR  200      32.291  39.292  13.763  1.00 25.45
ATOM   1505  CA  THR  200      31.050  38.585  13.510  1.00 25.65
ATOM   1506  CB  THR  200      30.261  39.193  12.339  1.00 25.75
ATOM   1507  OG1 THR  200      31.008  39.044  11.130  1.00 26.04
ATOM   1508  CG2 THR  200      30.002  40.672  12.573  1.00 26.48
ATOM   1509  C   THR  200      31.383  37.155  13.143  1.00 26.96
ATOM   1510  O   THR  200      30.832  36.211  13.712  1.00 27.62
ATOM   1511  N   VAL  201      32.295  36.990  12.189  1.00 28.07
ATOM   1512  CA  VAL  201      32.695  35.654  11.742  1.00 28.50
ATOM   1513  CB  VAL  201      33.785  35.726  10.665  1.00 29.26
ATOM   1514  CG1 VAL  201      34.056  34.332  10.123  1.00 31.22
ATOM   1515  CG2 VAL  201      33.370  36.684   9.546  1.00 27.90
ATOM   1516  C   VAL  201      33.231  34.818  12.901  1.00 29.16
ATOM   1517  O   VAL  201      32.816  33.676  13.101  1.00 29.44
ATOM   1518  N   ALA  202      34.156  35.395  13.663  1.00 30.31
ATOM   1519  CA  ALA  202      34.752  34.710  14.812  1.00 32.23
ATOM   1520  CB  ALA  202      35.591  35.705  15.643  1.00 31.72
ATOM   1521  C   ALA  202      33.688  34.070  15.696  1.00 33.37
ATOM   1522  O   ALA  202      33.789  32.894  16.073  1.00 34.14
ATOM   1523  N   THR  203      32.667  34.858  16.019  1.00 34.41
ATOM   1524  CA  THR  203      31.566  34.422  16.870  1.00 35.37
ATOM   1525  CB  THR  203      30.614  35.604  17.117  1.00 36.27
ATOM   1526  OG1 THR  203      31.370  36.708  17.645  1.00 37.04
ATOM   1527  CG2 THR  203      29.500  35.213  18.090  1.00 35.19
ATOM   1528  C   THR  203      30.800  33.260  16.242  1.00 36.08
ATOM   1529  O   THR  203      30.538  32.241  16.891  1.00 35.34
```

Figure 4

```
ATOM   1530  N   MSE  204      30.433  33.415  14.978  1.00 36.89
ATOM   1531  CA  MSE  204      29.722  32.348  14.299  1.00 37.94
ATOM   1532  CB  MSE  204      29.582  32.665  12.811  1.00 39.76
ATOM   1533  CG  MSE  204      29.065  31.504  11.954  1.00 40.74
ATOM   1534  SE  MSE  204      29.135  31.967  10.181  1.00 45.75
ATOM   1535  CE  MSE  204      30.643  31.057   9.627  1.00 45.26
ATOM   1536  C   MSE  204      30.531  31.075  14.465  1.00 38.36
ATOM   1537  O   MSE  204      30.024  30.064  14.954  1.00 37.86
ATOM   1538  N   ILE  205      31.798  31.148  14.061  1.00 38.79
ATOM   1539  CA  ILE  205      32.696  30.008  14.137  1.00 40.09
ATOM   1540  CB  ILE  205      34.178  30.451  13.981  1.00 39.81
ATOM   1541  CG2 ILE  205      35.098  29.240  14.072  1.00 39.47
ATOM   1542  CG1 ILE  205      34.398  31.112  12.616  1.00 39.46
ATOM   1543  CD1 ILE  205      34.250  30.158  11.425  1.00 39.34
ATOM   1544  C   ILE  205      32.527  29.215  15.440  1.00 41.84
ATOM   1545  O   ILE  205      32.121  28.050  15.408  1.00 41.41
ATOM   1546  N   SER  206      32.812  29.830  16.584  1.00 42.01
ATOM   1547  CA  SER  206      32.683  29.112  17.849  1.00 43.71
ATOM   1548  CB  SER  206      32.999  30.038  19.013  1.00 43.57
ATOM   1549  OG  SER  206      32.149  31.163  18.971  1.00 44.54
ATOM   1550  C   SER  206      31.306  28.494  18.056  1.00 44.83
ATOM   1551  O   SER  206      31.185  27.304  18.364  1.00 45.40
ATOM   1552  N   CYS  207      30.260  29.291  17.894  1.00 46.32
ATOM   1553  CA  CYS  207      28.912  28.764  18.079  1.00 48.14
ATOM   1554  CB  CYS  207      27.869  29.842  17.780  1.00 46.74
ATOM   1555  SG  CYS  207      27.946  31.264  18.883  1.00 42.50
ATOM   1556  C   CYS  207      28.666  27.551  17.186  1.00 50.79
ATOM   1557  O   CYS  207      27.715  26.799  17.403  1.00 50.97
ATOM   1558  N   TYR  208      29.533  27.361  16.190  1.00 53.91
ATOM   1559  CA  TYR  208      29.418  26.243  15.247  1.00 56.61
ATOM   1560  CB  TYR  208      30.350  26.458  14.045  1.00 56.96
ATOM   1561  CG  TYR  208      30.370  25.303  13.062  1.00 57.29
ATOM   1562  CD1 TYR  208      29.307  25.090  12.182  1.00 57.54
ATOM   1563  CE1 TYR  208      29.319  24.026  11.280  1.00 57.47
ATOM   1564  CD2 TYR  208      31.448  24.418  13.019  1.00 57.54
ATOM   1565  CE2 TYR  208      31.468  23.350  12.125  1.00 57.60
ATOM   1566  CZ  TYR  208      30.404  23.163  11.258  1.00 57.47
ATOM   1567  OH  TYR  208      30.435  22.126  10.360  1.00 57.71
ATOM   1568  C   TYR  208      29.705  24.867  15.854  1.00 58.12
ATOM   1569  O   TYR  208      28.874  23.960  15.773  1.00 58.61
ATOM   1570  N   TYR  209      30.876  24.699  16.459  1.00 59.77
ATOM   1571  CA  TYR  209      31.198  23.399  17.028  1.00 61.36
ATOM   1572  CB  TYR  209      32.619  23.394  17.581  1.00 63.23
ATOM   1573  CG  TYR  209      33.648  23.401  16.472  1.00 65.26
ATOM   1574  CD1 TYR  209      34.058  24.595  15.876  1.00 66.13
ATOM   1575  CE1 TYR  209      34.959  24.594  14.807  1.00 67.31
ATOM   1576  CD2 TYR  209      34.165  22.206  15.973  1.00 65.88
ATOM   1577  CE2 TYR  209      35.062  22.193  14.906  1.00 66.79
ATOM   1578  CZ  TYR  209      35.457  23.386  14.328  1.00 67.37
ATOM   1579  OH  TYR  209      36.350  23.370  13.277  1.00 67.62
ATOM   1580  C   TYR  209      30.206  22.965  18.083  1.00 61.32
ATOM   1581  O   TYR  209      30.048  21.771  18.336  1.00 61.19
ATOM   1582  N   GLU  210      29.523  23.938  18.680  1.00 61.63
ATOM   1583  CA  GLU  210      28.524  23.658  19.701  1.00 61.05
ATOM   1584  CB  GLU  210      28.444  24.808  20.706  1.00 62.29
ATOM   1585  CG  GLU  210      27.539  24.499  21.884  1.00 65.45
ATOM   1586  CD  GLU  210      27.716  25.463  23.050  1.00 67.38
ATOM   1587  OE1 GLU  210      28.865  25.609  23.535  1.00 68.93
ATOM   1588  OE2 GLU  210      26.707  26.065  23.488  1.00 67.92
```

Figure 4

```
ATOM   1589  C   GLU  210      27.175  23.459  19.026  1.00 60.04
ATOM   1590  O   GLU  210      26.255  22.901  19.618  1.00 59.93
ATOM   1591  N   ASP  211      27.073  23.920  17.780  1.00 58.82
ATOM   1592  CA  ASP  211      25.849  23.797  16.984  1.00 57.80
ATOM   1593  CB  ASP  211      24.804  24.824  17.441  1.00 58.16
ATOM   1594  CG  ASP  211      23.504  24.730  16.653  1.00 58.25
ATOM   1595  OD1 ASP  211      22.490  25.299  17.111  1.00 57.88
ATOM   1596  OD2 ASP  211      23.495  24.096  15.572  1.00 58.65
ATOM   1597  C   ASP  211      26.173  23.993  15.503  1.00 56.54
ATOM   1598  O   ASP  211      26.351  25.116  15.037  1.00 56.17
ATOM   1599  N   HIS  212      26.234  22.884  14.773  1.00 55.81
ATOM   1600  CA  HIS  212      26.577  22.884  13.351  1.00 55.26
ATOM   1601  CB  HIS  212      26.699  21.442  12.852  1.00 57.87
ATOM   1602  CG  HIS  212      27.816  20.678  13.493  1.00 61.52
ATOM   1603  CD2 HIS  212      27.815  19.527  14.205  1.00 62.63
ATOM   1604  ND1 HIS  212      29.127  21.110  13.460  1.00 62.80
ATOM   1605  CE1 HIS  212      29.884  20.258  14.127  1.00 63.70
ATOM   1606  NE2 HIS  212      29.114  19.288  14.590  1.00 63.71
ATOM   1607  C   HIS  212      25.665  23.656  12.412  1.00 53.29
ATOM   1608  O   HIS  212      26.014  23.883  11.251  1.00 52.77
ATOM   1609  N   GLN  213      24.496  24.058  12.895  1.00 51.08
ATOM   1610  CA  GLN  213      23.579  24.790  12.037  1.00 48.22
ATOM   1611  CB  GLN  213      22.135  24.347  12.298  1.00 49.39
ATOM   1612  CG  GLN  213      21.957  22.839  12.130  1.00 50.76
ATOM   1613  CD  GLN  213      20.507  22.410  11.965  1.00 51.82
ATOM   1614  OE1 GLN  213      19.653  22.721  12.803  1.00 52.48
ATOM   1615  NE2 GLN  213      20.223  21.679  10.883  1.00 51.72
ATOM   1616  C   GLN  213      23.746  26.289  12.202  1.00 45.19
ATOM   1617  O   GLN  213      22.978  27.077  11.654  1.00 45.00
ATOM   1618  N   CYS  214      24.759  26.686  12.957  1.00 41.87
ATOM   1619  CA  CYS  214      25.015  28.105  13.122  1.00 39.08
ATOM   1620  CB  CYS  214      25.907  28.386  14.332  1.00 39.18
ATOM   1621  SG  CYS  214      26.281  30.175  14.542  1.00 40.32
ATOM   1622  C   CYS  214      25.743  28.530  11.859  1.00 36.43
ATOM   1623  O   CYS  214      26.915  28.214  11.689  1.00 36.06
ATOM   1624  N   GLU  215      25.046  29.223  10.967  1.00 33.00
ATOM   1625  CA  GLU  215      25.664  29.672   9.736  1.00 30.60
ATOM   1626  CB  GLU  215      25.056  28.960   8.541  1.00 31.95
ATOM   1627  CG  GLU  215      25.289  27.466   8.561  1.00 33.57
ATOM   1628  CD  GLU  215      24.973  26.827   7.233  1.00 35.80
ATOM   1629  OE1 GLU  215      25.719  27.094   6.264  1.00 37.32
ATOM   1630  OE2 GLU  215      23.978  26.064   7.156  1.00 37.21
ATOM   1631  C   GLU  215      25.518  31.162   9.563  1.00 28.84
ATOM   1632  O   GLU  215      25.665  31.687   8.459  1.00 28.39
ATOM   1633  N   VAL  216      25.243  31.847  10.669  1.00 26.45
ATOM   1634  CA  VAL  216      25.083  33.291  10.648  1.00 23.67
ATOM   1635  CB  VAL  216      23.589  33.706  10.607  1.00 23.44
ATOM   1636  CG1 VAL  216      23.485  35.214  10.492  1.00 22.72
ATOM   1637  CG2 VAL  216      22.875  33.031   9.449  1.00 22.30
ATOM   1638  C   VAL  216      25.671  33.858  11.921  1.00 22.20
ATOM   1639  O   VAL  216      25.444  33.328  13.006  1.00 22.86
ATOM   1640  N   GLY  217      26.423  34.939  11.793  1.00 21.40
ATOM   1641  CA  GLY  217      26.997  35.554  12.965  1.00 21.14
ATOM   1642  C   GLY  217      26.524  36.994  13.022  1.00 22.30
ATOM   1643  O   GLY  217      26.432  37.677  11.983  1.00 22.05
ATOM   1644  N   MSE  218      26.201  37.454  14.228  1.00 23.03
ATOM   1645  CA  MSE  218      25.748  38.815  14.414  1.00 23.03
ATOM   1646  CB  MSE  218      24.208  38.880  14.445  1.00 25.98
ATOM   1647  CG  MSE  218      23.647  40.306  14.646  1.00 28.99
```

Figure 4

```
ATOM   1648  SE  MSE   218      21.806  40.486  14.543  1.00 35.34
ATOM   1649  CE  MSE   218      21.273  39.804  16.207  1.00 31.95
ATOM   1650  C   MSE   218      26.320  39.405  15.694  1.00 21.99
ATOM   1651  O   MSE   218      26.425  38.738  16.724  1.00 22.34
ATOM   1652  N   ILE   219      26.694  40.670  15.606  1.00 21.28
ATOM   1653  CA  ILE   219      27.240  41.402  16.720  1.00 20.85
ATOM   1654  CB  ILE   219      28.702  41.840  16.449  1.00 20.74
ATOM   1655  CG2 ILE   219      29.164  42.757  17.558  1.00 19.65
ATOM   1656  CG1 ILE   219      29.623  40.627  16.335  1.00 19.32
ATOM   1657  CD1 ILE   219      29.656  39.770  17.596  1.00 20.63
ATOM   1658  C   ILE   219      26.413  42.676  16.838  1.00 21.47
ATOM   1659  O   ILE   219      26.297  43.431  15.868  1.00 21.30
ATOM   1660  N   VAL   220      25.823  42.908  18.003  1.00 21.91
ATOM   1661  CA  VAL   220      25.059  44.135  18.224  1.00 22.49
ATOM   1662  CB  VAL   220      23.563  43.873  18.479  1.00 22.04
ATOM   1663  CG1 VAL   220      22.815  45.183  18.425  1.00 21.50
ATOM   1664  CG2 VAL   220      23.007  42.901  17.463  1.00 22.03
ATOM   1665  C   VAL   220      25.650  44.775  19.477  1.00 23.27
ATOM   1666  O   VAL   220      25.095  44.642  20.575  1.00 23.94
ATOM   1667  N   GLY   221      26.795  45.436  19.312  1.00 22.78
ATOM   1668  CA  GLY   221      27.448  46.063  20.443  1.00 22.86
ATOM   1669  C   GLY   221      27.728  47.509  20.138  1.00 23.75
ATOM   1670  O   GLY   221      26.816  48.264  19.828  1.00 25.09
ATOM   1671  N   THR   222      28.988  47.906  20.233  1.00 24.06
ATOM   1672  CA  THR   222      29.375  49.277  19.939  1.00 24.06
ATOM   1673  CB  THR   222      30.893  49.423  19.960  1.00 24.59
ATOM   1674  OG1 THR   222      31.377  49.051  21.258  1.00 26.00
ATOM   1675  CG2 THR   222      31.299  50.860  19.640  1.00 24.67
ATOM   1676  C   THR   222      28.888  49.530  18.533  1.00 24.09
ATOM   1677  O   THR   222      28.248  50.530  18.259  1.00 24.72
ATOM   1678  N   GLY   223      29.211  48.597  17.646  1.00 24.40
ATOM   1679  CA  GLY   223      28.790  48.686  16.262  1.00 24.65
ATOM   1680  C   GLY   223      27.797  47.560  16.020  1.00 25.05
ATOM   1681  O   GLY   223      27.478  46.779  16.936  1.00 25.80
ATOM   1682  N   CYS   224      27.298  47.453  14.798  1.00 24.73
ATOM   1683  CA  CYS   224      26.338  46.405  14.504  1.00 24.18
ATOM   1684  CB  CYS   224      24.928  46.958  14.682  1.00 24.47
ATOM   1685  SG  CYS   224      23.640  45.925  13.998  1.00 25.11
ATOM   1686  C   CYS   224      26.550  45.895  13.085  1.00 23.65
ATOM   1687  O   CYS   224      26.618  46.683  12.144  1.00 24.07
ATOM   1688  N   ASN   225      26.650  44.578  12.941  1.00 23.06
ATOM   1689  CA  ASN   225      26.883  43.963  11.638  1.00 23.27
ATOM   1690  CB  ASN   225      28.346  44.230  11.210  1.00 26.15
ATOM   1691  CG  ASN   225      28.831  43.296  10.098  1.00 27.94
ATOM   1692  OD1 ASN   225      28.271  43.265   8.997  1.00 29.23
ATOM   1693  ND2 ASN   225      29.878  42.524  10.393  1.00 28.62
ATOM   1694  C   ASN   225      26.603  42.459  11.740  1.00 21.80
ATOM   1695  O   ASN   225      26.291  41.954  12.827  1.00 20.54
ATOM   1696  N   ALA   226      26.709  41.759  10.610  1.00 19.99
ATOM   1697  CA  ALA   226      26.478  40.322  10.566  1.00 19.47
ATOM   1698  CB  ALA   226      24.994  40.032  10.443  1.00 20.99
ATOM   1699  C   ALA   226      27.194  39.723   9.378  1.00 18.72
ATOM   1700  O   ALA   226      27.529  40.428   8.415  1.00 17.97
ATOM   1701  N   CYS   227      27.404  38.415   9.439  1.00 18.36
ATOM   1702  CA  CYS   227      28.077  37.675   8.368  1.00 19.35
ATOM   1703  CB  CYS   227      29.523  37.396   8.751  1.00 18.42
ATOM   1704  SG  CYS   227      29.556  36.326  10.207  1.00 20.13
ATOM   1705  C   CYS   227      27.331  36.352   8.291  1.00 19.81
ATOM   1706  O   CYS   227      26.702  35.951   9.280  1.00 20.62
```

Figure 4

```
ATOM   1707  N   TYR  228      27.402  35.668   7.148  1.00 20.49
ATOM   1708  CA  TYR  228      26.705  34.384   6.989  1.00 20.56
ATOM   1709  CB  TYR  228      25.242  34.633   6.624  1.00 17.90
ATOM   1710  CG  TYR  228      25.096  35.134   5.204  1.00 15.65
ATOM   1711  CD1 TYR  228      24.922  34.249   4.145  1.00 15.81
ATOM   1712  CE1 TYR  228      24.885  34.701   2.823  1.00 15.89
ATOM   1713  CD2 TYR  228      25.221  36.483   4.913  1.00 15.28
ATOM   1714  CE2 TYR  228      25.186  36.949   3.601  1.00 16.08
ATOM   1715  CZ  TYR  228      25.022  36.051   2.564  1.00 16.76
ATOM   1716  OH  TYR  228      25.033  36.505   1.263  1.00 18.93
ATOM   1717  C   TYR  228      27.345  33.539   5.887  1.00 22.19
ATOM   1718  O   TYR  228      28.174  34.024   5.112  1.00 21.49
ATOM   1719  N   MSE  229      26.928  32.278   5.808  1.00 24.74
ATOM   1720  CA  MSE  229      27.438  31.349   4.808  1.00 26.69
ATOM   1721  CB  MSE  229      27.342  29.918   5.339  1.00 28.61
ATOM   1722  CG  MSE  229      28.167  29.637   6.598  1.00 32.37
ATOM   1723  SE  MSE  229      29.987  30.056   6.460  1.00 41.17
ATOM   1724  CE  MSE  229      30.544  28.874   5.098  1.00 36.30
ATOM   1725  C   MSE  229      26.663  31.470   3.481  1.00 27.83
ATOM   1726  O   MSE  229      25.535  30.994   3.363  1.00 28.02
ATOM   1727  N   GLU  230      27.282  32.109   2.492  1.00 29.19
ATOM   1728  CA  GLU  230      26.688  32.296   1.172  1.00 29.81
ATOM   1729  CB  GLU  230      27.165  33.623   0.577  1.00 30.83
ATOM   1730  CG  GLU  230      26.685  33.922  -0.843  1.00 32.33
ATOM   1731  CD  GLU  230      25.173  33.825  -0.989  1.00 34.04
ATOM   1732  OE1 GLU  230      24.663  32.698  -1.222  1.00 34.43
ATOM   1733  OE2 GLU  230      24.497  34.878  -0.858  1.00 33.65
ATOM   1734  C   GLU  230      27.127  31.143   0.282  1.00 30.91
ATOM   1735  O   GLU  230      27.958  30.319   0.685  1.00 30.80
ATOM   1736  N   GLU  231      26.562  31.078  -0.923  1.00 32.47
ATOM   1737  CA  GLU  231      26.885  30.024  -1.883  1.00 34.04
ATOM   1738  CB  GLU  231      25.668  29.696  -2.745  1.00 34.21
ATOM   1739  CG  GLU  231      24.408  29.396  -1.979  1.00 34.89
ATOM   1740  CD  GLU  231      24.452  28.054  -1.296  1.00 36.36
ATOM   1741  OE1 GLU  231      24.745  27.064  -2.002  1.00 36.80
ATOM   1742  OE2 GLU  231      24.182  27.981  -0.067  1.00 36.72
ATOM   1743  C   GLU  231      27.997  30.550  -2.777  1.00 35.65
ATOM   1744  O   GLU  231      27.889  31.663  -3.304  1.00 35.42
ATOM   1745  N   MSE  232      29.060  29.758  -2.952  1.00 37.13
ATOM   1746  CA  MSE  232      30.188  30.181  -3.780  1.00 38.19
ATOM   1747  CB  MSE  232      31.191  29.036  -3.935  1.00 41.27
ATOM   1748  CG  MSE  232      32.195  28.912  -2.765  1.00 45.40
ATOM   1749  SE  MSE  232      33.237  30.431  -2.467  1.00 52.07
ATOM   1750  CE  MSE  232      34.286  30.483  -3.969  1.00 48.20
ATOM   1751  C   MSE  232      29.694  30.664  -5.137  1.00 38.02
ATOM   1752  O   MSE  232      30.179  31.656  -5.678  1.00 36.84
ATOM   1753  N   GLN  233      28.698  29.970  -5.668  1.00 38.35
ATOM   1754  CA  GLN  233      28.110  30.331  -6.948  1.00 38.79
ATOM   1755  CB  GLN  233      26.954  29.373  -7.257  1.00 40.19
ATOM   1756  CG  GLN  233      25.658  30.041  -7.672  1.00 41.80
ATOM   1757  CD  GLN  233      24.460  29.119  -7.510  1.00 43.22
ATOM   1758  OE1 GLN  233      24.226  28.582  -6.424  1.00 44.27
ATOM   1759  NE2 GLN  233      23.688  28.936  -8.586  1.00 43.87
ATOM   1760  C   GLN  233      27.615  31.777  -6.936  1.00 38.45
ATOM   1761  O   GLN  233      27.495  32.407  -7.984  1.00 39.07
ATOM   1762  N   ASN  234      27.329  32.313  -5.753  1.00 37.79
ATOM   1763  CA  ASN  234      26.840  33.687  -5.668  1.00 36.56
ATOM   1764  CB  ASN  234      25.657  33.771  -4.706  1.00 37.03
ATOM   1765  CG  ASN  234      24.505  32.864  -5.119  1.00 36.83
```

Figure 4

```
ATOM   1766  OD1 ASN   234      24.152  32.793  -6.299  1.00 36.50
ATOM   1767  ND2 ASN   234      23.910  32.173  -4.146  1.00 36.25
ATOM   1768  C   ASN   234      27.919  34.676  -5.250  1.00 35.71
ATOM   1769  O   ASN   234      27.712  35.890  -5.301  1.00 35.11
ATOM   1770  N   VAL   235      29.069  34.156  -4.837  1.00 35.22
ATOM   1771  CA  VAL   235      30.177  35.009  -4.439  1.00 34.85
ATOM   1772  CB  VAL   235      31.056  34.321  -3.384  1.00 34.01
ATOM   1773  CG1 VAL   235      31.949  35.343  -2.717  1.00 32.35
ATOM   1774  CG2 VAL   235      30.185  33.576  -2.376  1.00 32.63
ATOM   1775  C   VAL   235      30.999  35.209  -5.706  1.00 35.79
ATOM   1776  O   VAL   235      32.011  34.548  -5.910  1.00 35.65
ATOM   1777  N   GLU   236      30.556  36.125  -6.556  1.00 37.55
ATOM   1778  CA  GLU   236      31.220  36.383  -7.830  1.00 39.52
ATOM   1779  CB  GLU   236      30.337  37.284  -8.701  1.00 39.67
ATOM   1780  CG  GLU   236      29.242  36.539  -9.448  1.00 41.02
ATOM   1781  CD  GLU   236      28.214  37.467 -10.072  1.00 42.58
ATOM   1782  OE1 GLU   236      28.607  38.529 -10.630  1.00 42.67
ATOM   1783  OE2 GLU   236      27.009  37.121 -10.011  1.00 43.02
ATOM   1784  C   GLU   236      32.631  36.961  -7.782  1.00 40.97
ATOM   1785  O   GLU   236      33.328  36.967  -8.803  1.00 42.27
ATOM   1786  N   LEU   237      33.064  37.457  -6.628  1.00 41.32
ATOM   1787  CA  LEU   237      34.408  38.017  -6.538  1.00 41.63
ATOM   1788  CB  LEU   237      34.438  39.163  -5.537  1.00 41.68
ATOM   1789  CG  LEU   237      33.545  40.367  -5.820  1.00 42.50
ATOM   1790  CD1 LEU   237      33.630  41.301  -4.623  1.00 44.17
ATOM   1791  CD2 LEU   237      33.984  41.101  -7.085  1.00 42.46
ATOM   1792  C   LEU   237      35.454  36.970  -6.148  1.00 42.43
ATOM   1793  O   LEU   237      36.636  37.294  -6.010  1.00 42.30
ATOM   1794  N   VAL   238      35.019  35.724  -5.967  1.00 42.96
ATOM   1795  CA  VAL   238      35.922  34.629  -5.606  1.00 43.89
ATOM   1796  CB  VAL   238      35.917  34.380  -4.097  1.00 42.33
ATOM   1797  CG1 VAL   238      36.722  33.136  -3.769  1.00 41.32
ATOM   1798  CG2 VAL   238      36.503  35.578  -3.385  1.00 42.74
ATOM   1799  C   VAL   238      35.520  33.337  -6.313  1.00 45.65
ATOM   1800  O   VAL   238      34.755  32.555  -5.770  1.00 46.15
ATOM   1801  N   GLU   239      36.069  33.116  -7.510  1.00 47.60
ATOM   1802  CA  GLU   239      35.769  31.947  -8.346  1.00 48.96
ATOM   1803  CB  GLU   239      36.819  31.793  -9.448  1.00 51.17
ATOM   1804  CG  GLU   239      37.000  33.026 -10.290  1.00 53.95
ATOM   1805  CD  GLU   239      37.817  34.066  -9.570  1.00 56.27
ATOM   1806  OE1 GLU   239      39.070  33.982  -9.637  1.00 58.40
ATOM   1807  OE2 GLU   239      37.211  34.950  -8.918  1.00 57.25
ATOM   1808  C   GLU   239      35.599  30.594  -7.675  1.00 48.87
ATOM   1809  O   GLU   239      36.272  30.274  -6.701  1.00 48.25
ATOM   1810  N   GLY   240      34.705  29.797  -8.252  1.00 49.09
ATOM   1811  CA  GLY   240      34.412  28.469  -7.750  1.00 50.05
ATOM   1812  C   GLY   240      32.967  28.418  -7.296  1.00 51.04
ATOM   1813  O   GLY   240      32.482  29.379  -6.712  1.00 52.00
ATOM   1814  N   ASP   241      32.259  27.332  -7.580  1.00 51.38
ATOM   1815  CA  ASP   241      30.882  27.214  -7.127  1.00 52.10
ATOM   1816  CB  ASP   241      29.963  26.766  -8.252  1.00 52.95
ATOM   1817  CG  ASP   241      30.186  27.534  -9.529  1.00 53.84
ATOM   1818  OD1 ASP   241      30.046  28.779  -9.522  1.00 53.20
ATOM   1819  OD2 ASP   241      30.496  26.875 -10.546  1.00 53.97
ATOM   1820  C   ASP   241      30.924  26.122  -6.083  1.00 52.90
ATOM   1821  O   ASP   241      29.898  25.563  -5.701  1.00 53.59
ATOM   1822  N   GLU   242      32.131  25.816  -5.626  1.00 53.45
ATOM   1823  CA  GLU   242      32.325  24.760  -4.646  1.00 53.65
ATOM   1824  CB  GLU   242      33.785  24.299  -4.670  1.00 55.19
```

Figure 4

```
ATOM   1825  CG  GLU  242      34.056  23.062  -3.826  1.00 57.57
ATOM   1826  CD  GLU  242      35.527  22.672  -3.811  1.00 58.85
ATOM   1827  OE1 GLU  242      36.063  22.340  -4.893  1.00 59.63
ATOM   1828  OE2 GLU  242      36.143  22.701  -2.717  1.00 59.85
ATOM   1829  C   GLU  242      31.933  25.159  -3.229  1.00 52.66
ATOM   1830  O   GLU  242      32.469  26.113  -2.661  1.00 53.15
ATOM   1831  N   GLY  243      30.987  24.418  -2.665  1.00 51.11
ATOM   1832  CA  GLY  243      30.545  24.673  -1.305  1.00 48.74
ATOM   1833  C   GLY  243      30.200  26.110  -0.967  1.00 46.87
ATOM   1834  O   GLY  243      29.879  26.917  -1.850  1.00 46.49
ATOM   1835  N   ARG  244      30.288  26.421   0.326  1.00 44.89
ATOM   1836  CA  ARG  244      29.967  27.748   0.838  1.00 43.27
ATOM   1837  CB  ARG  244      28.852  27.639   1.873  1.00 42.24
ATOM   1838  CG  ARG  244      27.571  27.040   1.339  1.00 42.16
ATOM   1839  CD  ARG  244      26.442  27.153   2.356  1.00 41.85
ATOM   1840  NE  ARG  244      25.254  26.425   1.925  1.00 39.30
ATOM   1841  CZ  ARG  244      24.702  25.446   2.630  1.00 39.15
ATOM   1842  NH1 ARG  244      25.236  25.085   3.794  1.00 38.10
ATOM   1843  NH2 ARG  244      23.627  24.821   2.168  1.00 38.77
ATOM   1844  C   ARG  244      31.121  28.524   1.465  1.00 42.34
ATOM   1845  O   ARG  244      32.089  27.945   1.958  1.00 41.77
ATOM   1846  N   MSE  245      30.990  29.849   1.446  1.00 42.07
ATOM   1847  CA  MSE  245      31.977  30.745   2.042  1.00 41.32
ATOM   1848  CB  MSE  245      32.846  31.391   0.974  1.00 42.25
ATOM   1849  CG  MSE  245      33.870  32.345   1.566  1.00 44.07
ATOM   1850  SE  MSE  245      34.884  33.206   0.332  1.00 47.16
ATOM   1851  CE  MSE  245      36.149  31.909  -0.005  1.00 44.40
ATOM   1852  C   MSE  245      31.324  31.863   2.863  1.00 40.37
ATOM   1853  O   MSE  245      30.525  32.644   2.338  1.00 40.13
ATOM   1854  N   CYS  246      31.664  31.940   4.148  1.00 38.95
ATOM   1855  CA  CYS  246      31.125  32.990   5.001  1.00 37.00
ATOM   1856  CB  CYS  246      31.794  32.953   6.376  1.00 37.69
ATOM   1857  SG  CYS  246      31.231  34.229   7.567  1.00 38.96
ATOM   1858  C   CYS  246      31.422  34.320   4.311  1.00 35.82
ATOM   1859  O   CYS  246      32.484  34.497   3.706  1.00 34.54
ATOM   1860  N   VAL  247      30.466  35.240   4.388  1.00 34.51
ATOM   1861  CA  VAL  247      30.591  36.566   3.782  1.00 32.46
ATOM   1862  CB  VAL  247      29.609  36.751   2.588  1.00 32.34
ATOM   1863  CG1 VAL  247      29.709  38.170   2.038  1.00 31.78
ATOM   1864  CG2 VAL  247      29.930  35.750   1.486  1.00 32.04
ATOM   1865  C   VAL  247      30.239  37.580   4.863  1.00 32.03
ATOM   1866  O   VAL  247      29.291  37.377   5.628  1.00 33.28
ATOM   1867  N   ASN  248      31.011  38.657   4.931  1.00 29.34
ATOM   1868  CA  ASN  248      30.792  39.699   5.917  1.00 27.36
ATOM   1869  CB  ASN  248      32.147  40.219   6.401  1.00 28.42
ATOM   1870  CG  ASN  248      32.031  41.471   7.253  1.00 29.34
ATOM   1871  OD1 ASN  248      30.975  41.774   7.816  1.00 29.82
ATOM   1872  ND2 ASN  248      33.141  42.201   7.374  1.00 29.54
ATOM   1873  C   ASN  248      29.983  40.798   5.257  1.00 27.10
ATOM   1874  O   ASN  248      30.531  41.618   4.503  1.00 26.98
ATOM   1875  N   THR  249      28.679  40.823   5.544  1.00 26.01
ATOM   1876  CA  THR  249      27.778  41.809   4.937  1.00 23.85
ATOM   1877  CB  THR  249      26.325  41.634   5.424  1.00 23.81
ATOM   1878  OG1 THR  249      26.228  42.100   6.775  1.00 25.10
ATOM   1879  CG2 THR  249      25.899  40.156   5.380  1.00 22.15
ATOM   1880  C   THR  249      28.208  43.226   5.270  1.00 24.20
ATOM   1881  O   THR  249      28.023  44.143   4.467  1.00 23.38
ATOM   1882  N   GLU  250      28.777  43.406   6.462  1.00 24.31
ATOM   1883  CA  GLU  250      29.219  44.733   6.891  1.00 23.61
```

Figure 4


```
ATOM   1884  CB  GLU  250      30.446  45.145   6.060  1.00 23.87
ATOM   1885  CG  GLU  250      31.242  46.362   6.571  1.00 25.94
ATOM   1886  CD  GLU  250      32.237  46.041   7.700  1.00 25.83
ATOM   1887  OE1 GLU  250      32.728  44.893   7.813  1.00 25.67
ATOM   1888  OE2 GLU  250      32.552  46.960   8.473  1.00 26.46
ATOM   1889  C   GLU  250      28.003  45.624   6.589  1.00 23.30
ATOM   1890  O   GLU  250      28.110  46.648   5.896  1.00 23.33
ATOM   1891  N   TRP  251      26.841  45.208   7.096  1.00 22.28
ATOM   1892  CA  TRP  251      25.609  45.940   6.840  1.00 22.36
ATOM   1893  CB  TRP  251      24.376  45.077   7.133  1.00 20.65
ATOM   1894  CG  TRP  251      24.133  44.726   8.543  1.00 18.29
ATOM   1895  CD2 TRP  251      23.308  43.648   9.016  1.00 16.51
ATOM   1896  CE2 TRP  251      23.279  43.725  10.424  1.00 15.08
ATOM   1897  CE3 TRP  251      22.589  42.635   8.384  1.00 16.17
ATOM   1898  CD1 TRP  251      24.565  45.395   9.652  1.00 17.71
ATOM   1899  NE1 TRP  251      24.051  44.795  10.795  1.00 17.10
ATOM   1900  CZ2 TRP  251      22.567  42.830  11.201  1.00 14.23
ATOM   1901  CZ3 TRP  251      21.872  41.737   9.171  1.00 15.72
ATOM   1902  CH2 TRP  251      21.869  41.842  10.559  1.00 14.23
ATOM   1903  C   TRP  251      25.445  47.283   7.523  1.00 23.49
ATOM   1904  O   TRP  251      24.541  48.044   7.167  1.00 23.95
ATOM   1905  N   GLY  252      26.302  47.579   8.500  1.00 24.44
ATOM   1906  CA  GLY  252      26.214  48.857   9.179  1.00 25.17
ATOM   1907  C   GLY  252      26.195  49.979   8.152  1.00 26.19
ATOM   1908  O   GLY  252      25.715  51.086   8.429  1.00 26.19
ATOM   1909  N   ALA  253      26.714  49.675   6.960  1.00 26.83
ATOM   1910  CA  ALA  253      26.791  50.622   5.851  1.00 27.86
ATOM   1911  CB  ALA  253      27.822  50.148   4.851  1.00 27.90
ATOM   1912  C   ALA  253      25.448  50.834   5.144  1.00 28.52
ATOM   1913  O   ALA  253      25.249  51.834   4.448  1.00 27.73
ATOM   1914  N   PHE  254      24.536  49.884   5.314  1.00 30.23
ATOM   1915  CA  PHE  254      23.224  49.974   4.696  1.00 31.42
ATOM   1916  CB  PHE  254      22.289  48.947   5.314  1.00 31.71
ATOM   1917  CG  PHE  254      20.899  48.995   4.768  1.00 31.90
ATOM   1918  CD1 PHE  254      20.655  48.736   3.429  1.00 31.47
ATOM   1919  CD2 PHE  254      19.824  49.273   5.600  1.00 32.95
ATOM   1920  CE1 PHE  254      19.367  48.746   2.927  1.00 31.38
ATOM   1921  CE2 PHE  254      18.518  49.285   5.096  1.00 32.69
ATOM   1922  CZ  PHE  254      18.295  49.021   3.763  1.00 31.47
ATOM   1923  C   PHE  254      22.664  51.367   4.928  1.00 32.56
ATOM   1924  O   PHE  254      22.638  51.839   6.064  1.00 33.19
ATOM   1925  N   GLY  255      22.227  52.017   3.849  1.00 33.62
ATOM   1926  CA  GLY  255      21.674  53.354   3.947  1.00 34.98
ATOM   1927  C   GLY  255      22.673  54.429   3.565  1.00 36.85
ATOM   1928  O   GLY  255      22.317  55.604   3.424  1.00 36.70
ATOM   1929  N   ASP  256      23.932  54.038   3.395  1.00 38.95
ATOM   1930  CA  ASP  256      24.966  55.000   3.038  1.00 41.47
ATOM   1931  CB  ASP  256      26.349  54.347   3.088  1.00 41.77
ATOM   1932  CG  ASP  256      26.880  54.224   4.502  1.00 42.36
ATOM   1933  OD1 ASP  256      26.573  55.120   5.322  1.00 43.08
ATOM   1934  OD2 ASP  256      27.617  53.251   4.791  1.00 42.28
ATOM   1935  C   ASP  256      24.744  55.636   1.666  1.00 43.10
ATOM   1936  O   ASP  256      25.489  56.533   1.261  1.00 44.08
ATOM   1937  N   SER  257      23.729  55.171   0.946  1.00 44.19
ATOM   1938  CA  SER  257      23.427  55.738  -0.363  1.00 45.32
ATOM   1939  CB  SER  257      23.714  54.713  -1.467  1.00 45.78
ATOM   1940  OG  SER  257      22.845  53.601  -1.375  1.00 46.48
ATOM   1941  C   SER  257      21.967  56.204  -0.423  1.00 45.41
ATOM   1942  O   SER  257      21.378  56.316  -1.501  1.00 46.14
```

Figure 4

	ATOM	1943	N	GLY	258	21.393	56.466	0.751	1.00	45.52
	ATOM	1944	CA	GLY	258	20.018	56.933	0.835	1.00	45.22
	ATOM	1945	C	GLY	258	18.922	55.896	1.042	1.00	45.11
	ATOM	1946	O	GLY	258	17.745	56.253	1.068	1.00	45.45
5	ATOM	1947	N	GLU	259	19.284	54.627	1.205	1.00	44.67
	ATOM	1948	CA	GLU	259	18.288	53.572	1.380	1.00	44.04
	ATOM	1949	CB	GLU	259	18.954	52.187	1.415	1.00	44.23
	ATOM	1950	CG	GLU	259	19.952	51.916	0.295	1.00	44.88
	ATOM	1951	CD	GLU	259	21.318	52.552	0.548	1.00	45.53
10	ATOM	1952	OE1	GLU	259	21.381	53.785	0.753	1.00	44.98
	ATOM	1953	OE2	GLU	259	22.335	51.817	0.537	1.00	45.95
	ATOM	1954	C	GLU	259	17.462	53.749	2.647	1.00	43.91
	ATOM	1955	O	GLU	259	16.461	53.061	2.836	1.00	43.49
	ATOM	1956	N	LEU	260	17.875	54.661	3.520	1.00	43.87
15	ATOM	1957	CA	LEU	260	17.143	54.865	4.765	1.00	44.40
	ATOM	1958	CB	LEU	260	18.023	54.513	5.967	1.00	44.36
	ATOM	1959	CG	LEU	260	18.398	53.041	6.153	1.00	44.87
	ATOM	1960	CD1	LEU	260	19.315	52.879	7.369	1.00	44.30
	ATOM	1961	CD2	LEU	260	17.127	52.216	6.307	1.00	44.88
20	ATOM	1962	C	LEU	260	16.632	56.282	4.932	1.00	44.59
	ATOM	1963	O	LEU	260	15.744	56.534	5.749	1.00	44.72
	ATOM	1964	N	ASP	261	17.200	57.202	4.161	1.00	44.48
	ATOM	1965	CA	ASP	261	16.821	58.608	4.234	1.00	44.18
	ATOM	1966	CB	ASP	261	16.813	59.224	2.841	1.00	44.99
25	ATOM	1967	CG	ASP	261	18.192	59.310	2.247	1.00	46.23
	ATOM	1968	OD1	ASP	261	19.165	58.994	2.980	1.00	46.42
	ATOM	1969	OD2	ASP	261	18.296	59.697	1.055	1.00	46.79
	ATOM	1970	C	ASP	261	15.482	58.885	4.892	1.00	43.00
	ATOM	1971	O	ASP	261	15.415	59.592	5.898	1.00	42.63
30	ATOM	1972	N	GLU	262	14.424	58.317	4.320	1.00	41.88
	ATOM	1973	CA	GLU	262	13.070	58.525	4.810	1.00	41.00
	ATOM	1974	CB	GLU	262	12.088	57.744	3.940	1.00	41.65
	ATOM	1975	CG	GLU	262	12.249	56.254	3.999	1.00	43.54
	ATOM	1976	CD	GLU	262	11.359	55.562	2.996	1.00	45.44
35	ATOM	1977	OE1	GLU	262	11.715	55.561	1.800	1.00	47.21
	ATOM	1978	OE2	GLU	262	10.296	55.031	3.391	1.00	47.29
	ATOM	1979	C	GLU	262	12.830	58.211	6.286	1.00	39.99
	ATOM	1980	O	GLU	262	11.997	58.852	6.918	1.00	40.22
	ATOM	1981	N	PHE	263	13.545	57.238	6.845	1.00	38.83
40	ATOM	1982	CA	PHE	263	13.360	56.908	8.258	1.00	37.00
	ATOM	1983	CB	PHE	263	13.684	55.430	8.512	1.00	34.37
	ATOM	1984	CG	PHE	263	12.828	54.476	7.717	1.00	32.41
	ATOM	1985	CD1	PHE	263	13.366	53.753	6.660	1.00	30.67
	ATOM	1986	CD2	PHE	263	11.474	54.317	8.012	1.00	30.95
45	ATOM	1987	CE1	PHE	263	12.567	52.886	5.909	1.00	29.82
	ATOM	1988	CE2	PHE	263	10.667	53.450	7.261	1.00	28.87
	ATOM	1989	CZ	PHE	263	11.214	52.737	6.213	1.00	29.09
	ATOM	1990	C	PHE	263	14.197	57.797	9.190	1.00	36.78
	ATOM	1991	O	PHE	263	13.809	58.041	10.327	1.00	37.58
50	ATOM	1992	N	LEU	264	15.328	58.301	8.712	1.00	36.72
	ATOM	1993	CA	LEU	264	16.193	59.142	9.542	1.00	37.11
	ATOM	1994	CB	LEU	264	17.389	59.638	8.725	1.00	36.98
	ATOM	1995	CG	LEU	264	18.131	58.621	7.852	1.00	36.59
	ATOM	1996	CD1	LEU	264	19.233	59.346	7.077	1.00	35.39
55	ATOM	1997	CD2	LEU	264	18.701	57.503	8.717	1.00	35.46
	ATOM	1998	C	LEU	264	15.482	60.350	10.158	1.00	37.28
	ATOM	1999	O	LEU	264	14.879	61.148	9.451	1.00	38.03
	ATOM	2000	N	LEU	265	15.574	60.480	11.479	1.00	37.63
	ATOM	2001	CA	LEU	265	14.965	61.585	12.215	1.00	37.33

Figure 4

ATOM	2002	CB	LEU	265	14.380	61.070	13.527	1.00	36.25
ATOM	2003	CG	LEU	265	13.529	59.807	13.417	1.00	35.76
ATOM	2004	CD1	LEU	265	13.157	59.295	14.808	1.00	35.17
ATOM	2005	CD2	LEU	265	12.292	60.120	12.598	1.00	35.59
ATOM	2006	C	LEU	265	16.054	62.613	12.521	1.00	38.22
ATOM	2007	O	LEU	265	17.239	62.285	12.486	1.00	38.34
ATOM	2008	N	GLU	266	15.653	63.844	12.832	1.00	39.22
ATOM	2009	CA	GLU	266	16.599	64.922	13.137	1.00	40.56
ATOM	2010	CB	GLU	266	15.874	66.101	13.813	1.00	41.82
ATOM	2011	CG	GLU	266	15.277	65.777	15.196	1.00	44.28
ATOM	2012	CD	GLU	266	14.612	66.974	15.886	1.00	44.95
ATOM	2013	OE1	GLU	266	13.543	67.432	15.410	1.00	45.08
ATOM	2014	OE2	GLU	266	15.163	67.452	16.910	1.00	45.53
ATOM	2015	C	GLU	266	17.733	64.435	14.036	1.00	40.54
ATOM	2016	O	GLU	266	18.910	64.657	13.750	1.00	40.69
ATOM	2017	N	TYR	267	17.366	63.760	15.121	1.00	40.61
ATOM	2018	CA	TYR	267	18.342	63.234	16.062	1.00	40.30
ATOM	2019	CB	TYR	267	17.639	62.364	17.110	1.00	39.44
ATOM	2020	CG	TYR	267	16.216	62.784	17.423	1.00	38.98
ATOM	2021	CD1	TYR	267	15.134	61.967	17.066	1.00	38.66
ATOM	2022	CE1	TYR	267	13.813	62.342	17.349	1.00	38.28
ATOM	2023	CD2	TYR	267	15.943	63.995	18.075	1.00	38.72
ATOM	2024	CE2	TYR	267	14.619	64.381	18.364	1.00	38.45
ATOM	2025	CZ	TYR	267	13.564	63.548	17.996	1.00	38.30
ATOM	2026	OH	TYR	267	12.267	63.923	18.251	1.00	37.22
ATOM	2027	C	TYR	267	19.381	62.403	15.296	1.00	40.27
ATOM	2028	O	TYR	267	20.580	62.469	15.579	1.00	40.14
ATOM	2029	N	ASP	268	18.909	61.626	14.324	1.00	40.61
ATOM	2030	CA	ASP	268	19.781	60.790	13.511	1.00	40.87
ATOM	2031	CB	ASP	268	18.946	59.920	12.566	1.00	39.36
ATOM	2032	CG	ASP	268	18.183	58.843	13.301	1.00	38.52
ATOM	2033	OD1	ASP	268	18.819	58.118	14.082	1.00	39.79
ATOM	2034	OD2	ASP	268	16.961	58.711	13.110	1.00	36.13
ATOM	2035	C	ASP	268	20.764	61.643	12.712	1.00	41.97
ATOM	2036	O	ASP	268	21.956	61.339	12.667	1.00	42.91
ATOM	2037	N	ARG	269	20.266	62.710	12.090	1.00	42.73
ATOM	2038	CA	ARG	269	21.113	63.606	11.310	1.00	43.23
ATOM	2039	CB	ARG	269	20.302	64.793	10.786	1.00	45.34
ATOM	2040	CG	ARG	269	18.923	64.464	10.223	1.00	47.46
ATOM	2041	CD	ARG	269	19.000	63.819	8.864	1.00	49.22
ATOM	2042	NE	ARG	269	17.667	63.552	8.337	1.00	52.67
ATOM	2043	CZ	ARG	269	17.426	62.969	7.165	1.00	54.63
ATOM	2044	NH1	ARG	269	18.436	62.591	6.386	1.00	55.41
ATOM	2045	NH2	ARG	269	16.173	62.747	6.775	1.00	55.38
ATOM	2046	C	ARG	269	22.204	64.150	12.231	1.00	42.99
ATOM	2047	O	ARG	269	23.400	63.999	11.977	1.00	43.63
ATOM	2048	N	LEU	270	21.777	64.796	13.305	1.00	41.99
ATOM	2049	CA	LEU	270	22.702	65.372	14.261	1.00	41.33
ATOM	2050	CB	LEU	270	21.924	65.812	15.502	1.00	41.15
ATOM	2051	CG	LEU	270	21.004	67.002	15.217	1.00	40.34
ATOM	2052	CD1	LEU	270	19.964	67.182	16.307	1.00	39.94
ATOM	2053	CD2	LEU	270	21.879	68.237	15.084	1.00	40.26
ATOM	2054	C	LEU	270	23.828	64.406	14.635	1.00	41.26
ATOM	2055	O	LEU	270	25.009	64.762	14.553	1.00	41.76
ATOM	2056	N	VAL	271	23.462	63.188	15.030	1.00	40.24
ATOM	2057	CA	VAL	271	24.443	62.177	15.415	1.00	40.08
ATOM	2058	CB	VAL	271	23.776	60.838	15.730	1.00	40.42
ATOM	2059	CG1	VAL	271	24.846	59.800	16.050	1.00	39.86
ATOM	2060	CG2	VAL	271	22.796	61.000	16.891	1.00	40.86

Figure 4

	ATOM	2061	C	VAL	271	25.477	61.903	14.329	1.00	40.51
	ATOM	2062	O	VAL	271	26.676	61.832	14.595	1.00	40.15
	ATOM	2063	N	ASP	272	24.998	61.730	13.103	1.00	40.78
	ATOM	2064	CA	ASP	272	25.866	61.447	11.977	1.00	40.36
5	ATOM	2065	CB	ASP	272	25.038	61.344	10.695	1.00	39.16
	ATOM	2066	CG	ASP	272	25.792	60.670	9.553	1.00	38.09
	ATOM	2067	OD1	ASP	272	26.821	60.000	9.807	1.00	36.54
	ATOM	2068	OD2	ASP	272	25.335	60.798	8.394	1.00	37.12
	ATOM	2069	C	ASP	272	26.901	62.544	11.849	1.00	40.88
10	ATOM	2070	O	ASP	272	28.099	62.297	11.953	1.00	40.75
	ATOM	2071	N	GLU	273	26.429	63.763	11.638	1.00	41.96
	ATOM	2072	CA	GLU	273	27.321	64.896	11.477	1.00	43.14
	ATOM	2073	CB	GLU	273	26.501	66.170	11.470	1.00	44.13
	ATOM	2074	CG	GLU	273	25.576	66.214	10.272	1.00	46.73
15	ATOM	2075	CD	GLU	273	24.629	67.388	10.308	1.00	48.40
	ATOM	2076	OE1	GLU	273	25.047	68.455	10.828	1.00	49.15
	ATOM	2077	OE2	GLU	273	23.482	67.241	9.811	1.00	48.64
	ATOM	2078	C	GLU	273	28.428	64.968	12.517	1.00	43.48
	ATOM	2079	O	GLU	273	29.575	65.279	12.187	1.00	43.59
20	ATOM	2080	N	SER	274	28.095	64.666	13.767	1.00	44.05
	ATOM	2081	CA	SER	274	29.089	64.702	14.837	1.00	44.54
	ATOM	2082	CB	SER	274	28.421	64.568	16.205	1.00	45.39
	ATOM	2083	OG	SER	274	27.496	65.611	16.424	1.00	48.14
	ATOM	2084	C	SER	274	30.106	63.582	14.694	1.00	44.23
25	ATOM	2085	O	SER	274	31.292	63.783	14.931	1.00	44.76
	ATOM	2086	N	SER	275	29.632	62.400	14.318	1.00	43.84
	ATOM	2087	CA	SER	275	30.489	61.227	14.162	1.00	43.42
	ATOM	2088	CB	SER	275	29.754	60.139	13.392	1.00	43.28
	ATOM	2089	OG	SER	275	29.758	60.444	12.010	1.00	42.94
30	ATOM	2090	C	SER	275	31.789	61.535	13.426	1.00	43.34
	ATOM	2091	O	SER	275	31.914	62.552	12.738	1.00	43.76
	ATOM	2092	N	ALA	276	32.756	60.639	13.570	1.00	42.68
	ATOM	2093	CA	ALA	276	34.034	60.805	12.906	1.00	42.98
	ATOM	2094	CB	ALA	276	35.108	60.015	13.639	1.00	42.92
35	ATOM	2095	C	ALA	276	33.930	60.319	11.465	1.00	43.23
	ATOM	2096	O	ALA	276	34.936	60.277	10.751	1.00	44.60
	ATOM	2097	N	ASN	277	32.722	59.949	11.039	1.00	42.10
	ATOM	2098	CA	ASN	277	32.517	59.447	9.691	1.00	40.87
	ATOM	2099	CB	ASN	277	32.615	57.927	9.685	1.00	41.63
40	ATOM	2100	CG	ASN	277	31.654	57.283	10.659	1.00	42.64
	ATOM	2101	OD1	ASN	277	30.670	57.898	11.067	1.00	43.50
	ATOM	2102	ND2	ASN	277	31.925	56.033	11.029	1.00	42.98
	ATOM	2103	C	ASN	277	31.178	59.865	9.104	1.00	40.57
	ATOM	2104	O	ASN	277	30.430	59.039	8.579	1.00	39.89
45	ATOM	2105	N	PRO	278	30.868	61.163	9.163	1.00	40.83
	ATOM	2106	CD	PRO	278	31.783	62.282	9.451	1.00	40.90
	ATOM	2107	CA	PRO	278	29.600	61.657	8.623	1.00	40.71
	ATOM	2108	CB	PRO	278	29.807	63.175	8.579	1.00	40.88
	ATOM	2109	CG	PRO	278	31.303	63.326	8.474	1.00	41.27
50	ATOM	2110	C	PRO	278	29.239	61.074	7.258	1.00	40.60
	ATOM	2111	O	PRO	278	29.949	61.284	6.270	1.00	40.71
	ATOM	2112	N	GLY	279	28.131	60.338	7.216	1.00	40.34
	ATOM	2113	CA	GLY	279	27.676	59.747	5.971	1.00	39.10
	ATOM	2114	C	GLY	279	27.904	58.252	5.828	1.00	38.94
55	ATOM	2115	O	GLY	279	27.315	57.635	4.952	1.00	39.74
	ATOM	2116	N	GLN	280	28.735	57.660	6.683	1.00	38.66
	ATOM	2117	CA	GLN	280	29.049	56.230	6.605	1.00	37.75
	ATOM	2118	CB	GLN	280	30.563	56.043	6.513	1.00	37.97
	ATOM	2119	CG	GLN	280	31.243	56.954	5.509	1.00	39.85

Figure 4

	ATOM	2120	CD	GLN	280	32.743	57.046	5.730	1.00	40.76
	ATOM	2121	OE1	GLN	280	33.465	56.058	5.587	1.00	41.39
	ATOM	2122	NE2	GLN	280	33.220	58.240	6.083	1.00	41.57
	ATOM	2123	C	GLN	280	28.553	55.455	7.817	1.00	36.99
5	ATOM	2124	O	GLN	280	28.645	55.939	8.941	1.00	37.89
	ATOM	2125	N	GLN	281	28.054	54.242	7.592	1.00	35.75
	ATOM	2126	CA	GLN	281	27.572	53.401	8.681	1.00	34.04
	ATOM	2127	CB	GLN	281	28.590	53.404	9.829	1.00	33.35
	ATOM	2128	CG	GLN	281	29.971	52.951	9.447	1.00	33.09
10	ATOM	2129	CD	GLN	281	29.967	51.576	8.800	1.00	34.44
	ATOM	2130	OE1	GLN	281	29.917	51.451	7.572	1.00	33.95
	ATOM	2131	NE2	GLN	281	30.000	50.529	9.630	1.00	34.63
	ATOM	2132	C	GLN	281	26.210	53.831	9.237	1.00	33.42
	ATOM	2133	O	GLN	281	25.895	53.530	10.390	1.00	34.87
15	ATOM	2134	N	LEU	282	25.395	54.511	8.436	1.00	31.53
	ATOM	2135	CA	LEU	282	24.098	54.992	8.913	1.00	29.87
	ATOM	2136	CB	LEU	282	23.345	55.685	7.777	1.00	30.15
	ATOM	2137	CG	LEU	282	24.030	56.871	7.085	1.00	30.41
	ATOM	2138	CD1	LEU	282	22.963	57.741	6.435	1.00	29.82
20	ATOM	2139	CD2	LEU	282	24.815	57.699	8.097	1.00	30.66
	ATOM	2140	C	LEU	282	23.191	53.949	9.578	1.00	28.70
	ATOM	2141	O	LEU	282	22.716	54.153	10.698	1.00	28.78
	ATOM	2142	N	TYR	283	22.935	52.841	8.894	1.00	27.35
	ATOM	2143	CA	TYR	283	22.095	51.793	9.461	1.00	26.53
25	ATOM	2144	CB	TYR	283	22.233	50.511	8.633	1.00	24.41
	ATOM	2145	CG	TYR	283	21.420	49.338	9.143	1.00	22.90
	ATOM	2146	CD1	TYR	283	20.021	49.413	9.210	1.00	21.94
	ATOM	2147	CE1	TYR	283	19.257	48.318	9.609	1.00	20.96
	ATOM	2148	CD2	TYR	283	22.038	48.129	9.503	1.00	21.53
30	ATOM	2149	CE2	TYR	283	21.279	47.030	9.907	1.00	20.87
	ATOM	2150	CZ	TYR	283	19.886	47.140	9.950	1.00	21.33
	ATOM	2151	OH	TYR	283	19.105	46.068	10.310	1.00	23.85
	ATOM	2152	C	TYR	283	22.567	51.532	10.891	1.00	27.12
	ATOM	2153	O	TYR	283	21.783	51.521	11.841	1.00	28.95
35	ATOM	2154	N	GLU	284	23.869	51.352	11.035	1.00	26.60
	ATOM	2155	CA	GLU	284	24.486	51.072	12.317	1.00	26.43
	ATOM	2156	CB	GLU	284	25.982	50.905	12.108	1.00	27.03
	ATOM	2157	CG	GLU	284	26.763	50.680	13.375	1.00	27.21
	ATOM	2158	CD	GLU	284	28.224	50.492	13.082	1.00	27.57
40	ATOM	2159	OE1	GLU	284	28.897	51.506	12.734	1.00	27.02
	ATOM	2160	OE2	GLU	284	28.670	49.319	13.185	1.00	26.30
	ATOM	2161	C	GLU	284	24.249	52.133	13.381	1.00	26.81
	ATOM	2162	O	GLU	284	24.197	51.826	14.582	1.00	26.06
	ATOM	2163	N	LYS	285	24.134	53.384	12.940	1.00	27.07
45	ATOM	2164	CA	LYS	285	23.926	54.502	13.860	1.00	27.39
	ATOM	2165	CB	LYS	285	24.339	55.825	13.186	1.00	25.99
	ATOM	2166	CG	LYS	285	25.840	56.012	13.132	1.00	24.13
	ATOM	2167	CD	LYS	285	26.235	57.110	12.179	1.00	23.29
	ATOM	2168	CE	LYS	285	27.755	57.193	12.052	1.00	22.03
50	ATOM	2169	NZ	LYS	285	28.142	58.198	11.027	1.00	21.72
	ATOM	2170	C	LYS	285	22.488	54.595	14.368	1.00	28.05
	ATOM	2171	O	LYS	285	22.086	55.615	14.941	1.00	28.61
	ATOM	2172	N	LEU	286	21.717	53.535	14.144	1.00	27.60
	ATOM	2173	CA	LEU	286	20.335	53.488	14.599	1.00	27.30
55	ATOM	2174	CB	LEU	286	19.399	53.157	13.435	1.00	28.57
	ATOM	2175	CG	LEU	286	19.375	54.167	12.279	1.00	30.25
	ATOM	2176	CD1	LEU	286	18.480	53.647	11.139	1.00	29.98
	ATOM	2177	CD2	LEU	286	18.863	55.507	12.780	1.00	29.35
	ATOM	2178	C	LEU	286	20.260	52.381	15.632	1.00	27.01

Figure 4

```
ATOM   2179  O   LEU  286      19.296  52.294  16.399  1.00 27.55
ATOM   2180  N   ILE  287      21.306  51.554  15.645  1.00 26.00
ATOM   2181  CA  ILE  287      21.415  50.399  16.532  1.00 24.38
ATOM   2182  CB  ILE  287      21.551  49.141  15.715  1.00 23.92
ATOM   2183  CG2 ILE  287      21.470  47.919  16.628  1.00 22.70
ATOM   2184  CG1 ILE  287      20.510  49.158  14.597  1.00 22.87
ATOM   2185  CD1 ILE  287      20.676  48.042  13.607  1.00 22.79
ATOM   2186  C   ILE  287      22.639  50.444  17.433  1.00 24.65
ATOM   2187  O   ILE  287      22.550  50.255  18.644  1.00 23.54
ATOM   2188  N   GLY  288      23.791  50.668  16.810  1.00 25.94
ATOM   2189  CA  GLY  288      25.060  50.714  17.519  1.00 26.86
ATOM   2190  C   GLY  288      25.081  51.266  18.927  1.00 27.76
ATOM   2191  O   GLY  288      24.697  52.412  19.164  1.00 28.19
ATOM   2192  N   GLY  289      25.554  50.445  19.860  1.00 28.95
ATOM   2193  CA  GLY  289      25.656  50.856  21.249  1.00 30.64
ATOM   2194  C   GLY  289      26.632  52.007  21.407  1.00 31.92
ATOM   2195  O   GLY  289      26.930  52.442  22.509  1.00 32.56
ATOM   2196  N   LYS  290      27.133  52.504  20.291  1.00 32.83
ATOM   2197  CA  LYS  290      28.067  53.607  20.296  1.00 33.99
ATOM   2198  CB  LYS  290      29.104  53.373  19.191  1.00 35.04
ATOM   2199  CG  LYS  290      29.858  54.598  18.665  1.00 36.71
ATOM   2200  CD  LYS  290      31.032  54.996  19.551  1.00 38.80
ATOM   2201  CE  LYS  290      31.936  56.011  18.839  1.00 39.77
ATOM   2202  NZ  LYS  290      32.864  56.707  19.787  1.00 41.04
ATOM   2203  C   LYS  290      27.278  54.880  20.035  1.00 34.58
ATOM   2204  O   LYS  290      27.810  55.984  20.138  1.00 35.79
ATOM   2205  N   TYR  291      26.001  54.734  19.708  1.00 33.80
ATOM   2206  CA  TYR  291      25.196  55.907  19.406  1.00 33.61
ATOM   2207  CB  TYR  291      25.010  56.046  17.892  1.00 33.22
ATOM   2208  CG  TYR  291      26.256  55.752  17.084  1.00 33.77
ATOM   2209  CD1 TYR  291      26.659  54.435  16.838  1.00 34.23
ATOM   2210  CE1 TYR  291      27.789  54.155  16.065  1.00 34.17
ATOM   2211  CD2 TYR  291      27.021  56.783  16.542  1.00 33.61
ATOM   2212  CE2 TYR  291      28.150  56.515  15.773  1.00 33.54
ATOM   2213  CZ  TYR  291      28.528  55.200  15.532  1.00 33.76
ATOM   2214  OH  TYR  291      29.620  54.928  14.729  1.00 34.36
ATOM   2215  C   TYR  291      23.836  55.874  20.070  1.00 33.11
ATOM   2216  O   TYR  291      23.069  56.828  19.975  1.00 32.86
ATOM   2217  N   MSE  292      23.521  54.778  20.737  1.00 33.27
ATOM   2218  CA  MSE  292      22.230  54.699  21.389  1.00 33.18
ATOM   2219  CB  MSE  292      22.066  53.349  22.062  1.00 33.77
ATOM   2220  CG  MSE  292      20.639  52.975  22.314  1.00 35.15
ATOM   2221  SE  MSE  292      20.564  51.230  22.803  1.00 41.54
ATOM   2222  CE  MSE  292      20.269  50.385  21.171  1.00 35.91
ATOM   2223  C   MSE  292      22.148  55.818  22.423  1.00 32.97
ATOM   2224  O   MSE  292      21.227  56.637  22.400  1.00 33.49
ATOM   2225  N   GLY  293      23.131  55.861  23.315  1.00 32.96
ATOM   2226  CA  GLY  293      23.151  56.892  24.334  1.00 32.25
ATOM   2227  C   GLY  293      23.067  58.290  23.750  1.00 32.18
ATOM   2228  O   GLY  293      22.307  59.126  24.241  1.00 33.24
ATOM   2229  N   GLU  294      23.835  58.560  22.702  1.00 31.47
ATOM   2230  CA  GLU  294      23.809  59.883  22.096  1.00 31.38
ATOM   2231  CB  GLU  294      24.875  59.971  21.008  1.00 33.29
ATOM   2232  CG  GLU  294      24.986  61.321  20.304  1.00 34.67
ATOM   2233  CD  GLU  294      25.227  62.474  21.257  1.00 35.80
ATOM   2234  OE1 GLU  294      25.708  62.244  22.389  1.00 36.49
ATOM   2235  OE2 GLU  294      24.946  63.623  20.858  1.00 37.16
ATOM   2236  C   GLU  294      22.428  60.192  21.521  1.00 30.62
ATOM   2237  O   GLU  294      21.919  61.305  21.664  1.00 30.94
```

	ATOM	2238	N	LEU	295	21.818	59.204	20.878	1.00	29.56
	ATOM	2239	CA	LEU	295	20.495	59.392	20.303	1.00	29.24
	ATOM	2240	CB	LEU	295	20.030	58.112	19.589	1.00	27.27
	ATOM	2241	CG	LEU	295	20.389	58.007	18.099	1.00	25.46
5	ATOM	2242	CD1	LEU	295	19.979	56.668	17.522	1.00	21.87
	ATOM	2243	CD2	LEU	295	19.677	59.136	17.352	1.00	25.71
	ATOM	2244	C	LEU	295	19.497	59.787	21.388	1.00	29.98
	ATOM	2245	O	LEU	295	18.587	60.573	21.156	1.00	30.19
	ATOM	2246	N	VAL	296	19.665	59.250	22.585	1.00	31.23
10	ATOM	2247	CA	VAL	296	18.745	59.590	23.657	1.00	32.87
	ATOM	2248	CB	VAL	296	18.890	58.623	24.831	1.00	32.48
	ATOM	2249	CG1	VAL	296	17.827	58.899	25.868	1.00	32.99
	ATOM	2250	CG2	VAL	296	18.762	57.198	24.323	1.00	33.56
	ATOM	2251	C	VAL	296	19.020	61.025	24.122	1.00	33.74
15	ATOM	2252	O	VAL	296	18.086	61.778	24.431	1.00	33.68
	ATOM	2253	N	ARG	297	20.296	61.409	24.145	1.00	34.02
	ATOM	2254	CA	ARG	297	20.659	62.757	24.563	1.00	35.34
	ATOM	2255	CB	ARG	297	22.147	63.008	24.342	1.00	34.89
	ATOM	2256	CG	ARG	297	22.940	63.279	25.609	1.00	35.27
20	ATOM	2257	CD	ARG	297	23.791	64.525	25.454	1.00	35.98
	ATOM	2258	NE	ARG	297	24.226	64.700	24.074	1.00	37.11
	ATOM	2259	CZ	ARG	297	24.476	65.878	23.513	1.00	37.43
	ATOM	2260	NH1	ARG	297	24.348	66.994	24.226	1.00	38.45
	ATOM	2261	NH2	ARG	297	24.809	65.944	22.229	1.00	36.61
25	ATOM	2262	C	ARG	297	19.870	63.766	23.747	1.00	36.07
	ATOM	2263	O	ARG	297	19.103	64.574	24.285	1.00	36.76
	ATOM	2264	N	LEU	298	20.063	63.699	22.437	1.00	36.93
	ATOM	2265	CA	LEU	298	19.407	64.596	21.500	1.00	37.55
	ATOM	2266	CB	LEU	298	19.768	64.178	20.077	1.00	37.28
30	ATOM	2267	CG	LEU	298	21.272	64.065	19.816	1.00	36.13
	ATOM	2268	CD1	LEU	298	21.478	63.784	18.341	1.00	36.85
	ATOM	2269	CD2	LEU	298	21.991	65.356	20.218	1.00	35.02
	ATOM	2270	C	LEU	298	17.892	64.633	21.670	1.00	38.53
	ATOM	2271	O	LEU	298	17.276	65.708	21.618	1.00	38.44
35	ATOM	2272	N	VAL	299	17.289	63.462	21.866	1.00	39.23
	ATOM	2273	CA	VAL	299	15.839	63.389	22.054	1.00	40.08
	ATOM	2274	CB	VAL	299	15.349	61.932	22.110	1.00	39.44
	ATOM	2275	CG1	VAL	299	13.844	61.892	22.385	1.00	37.91
	ATOM	2276	CG2	VAL	299	15.676	61.240	20.802	1.00	38.72
40	ATOM	2277	C	VAL	299	15.435	64.087	23.350	1.00	40.94
	ATOM	2278	O	VAL	299	14.321	64.612	23.461	1.00	41.66
	ATOM	2279	N	LEU	300	16.337	64.091	24.328	1.00	41.41
	ATOM	2280	CA	LEU	300	16.043	64.737	25.600	1.00	42.31
	ATOM	2281	CB	LEU	300	16.973	64.224	26.713	1.00	41.48
45	ATOM	2282	CG	LEU	300	16.943	62.766	27.206	1.00	40.38
	ATOM	2283	CD1	LEU	300	17.677	62.711	28.545	1.00	40.14
	ATOM	2284	CD2	LEU	300	15.517	62.251	27.380	1.00	38.74
	ATOM	2285	C	LEU	300	16.204	66.251	25.444	1.00	43.44
	ATOM	2286	O	LEU	300	15.304	67.020	25.806	1.00	43.84
50	ATOM	2287	N	LEU	301	17.346	66.675	24.898	1.00	43.90
	ATOM	2288	CA	LEU	301	17.603	68.100	24.707	1.00	43.85
	ATOM	2289	CB	LEU	301	18.895	68.335	23.919	1.00	43.20
	ATOM	2290	CG	LEU	301	20.211	67.969	24.613	1.00	43.48
	ATOM	2291	CD1	LEU	301	21.385	68.372	23.730	1.00	43.37
55	ATOM	2292	CD2	LEU	301	20.307	68.675	25.955	1.00	43.71
	ATOM	2293	C	LEU	301	16.444	68.738	23.969	1.00	44.11
	ATOM	2294	O	LEU	301	16.068	69.875	24.254	1.00	44.38
	ATOM	2295	N	ARG	302	15.863	68.007	23.025	1.00	44.45
	ATOM	2296	CA	ARG	302	14.753	68.571	22.280	1.00	45.04

Figure 4


```
ATOM   2297  CB  ARG  302      14.296  67.660  21.148  1.00 45.49
ATOM   2298  CG  ARG  302      13.082  68.256  20.468  1.00 45.91
ATOM   2299  CD  ARG  302      12.391  67.327  19.514  1.00 46.45
ATOM   2300  NE  ARG  302      11.194  67.985  19.007  1.00 47.37
ATOM   2301  CZ  ARG  302      10.423  67.503  18.043  1.00 48.12
ATOM   2302  NH1 ARG  302      10.719  66.344  17.466  1.00 48.80
ATOM   2303  NH2 ARG  302       9.357  68.190  17.657  1.00 47.77
ATOM   2304  C   ARG  302      13.577  68.807  23.196  1.00 45.13
ATOM   2305  O   ARG  302      12.982  69.885  23.198  1.00 45.57
ATOM   2306  N   LEU  303      13.228  67.787  23.966  1.00 45.14
ATOM   2307  CA  LEU  303      12.113  67.918  24.883  1.00 45.18
ATOM   2308  CB  LEU  303      11.952  66.624  25.695  1.00 44.02
ATOM   2309  CG  LEU  303      11.495  65.427  24.846  1.00 42.43
ATOM   2310  CD1 LEU  303      11.365  64.162  25.690  1.00 41.06
ATOM   2311  CD2 LEU  303      10.154  65.784  24.207  1.00 41.96
ATOM   2312  C   LEU  303      12.359  69.133  25.783  1.00 45.83
ATOM   2313  O   LEU  303      11.444  69.919  26.044  1.00 45.85
ATOM   2314  N   VAL  304      13.599  69.302  26.232  1.00 46.44
ATOM   2315  CA  VAL  304      13.943  70.440  27.085  1.00 47.76
ATOM   2316  CB  VAL  304      15.443  70.426  27.496  1.00 47.79
ATOM   2317  CG1 VAL  304      15.866  71.815  27.996  1.00 46.89
ATOM   2318  CG2 VAL  304      15.678  69.386  28.581  1.00 47.81
ATOM   2319  C   VAL  304      13.666  71.764  26.371  1.00 48.44
ATOM   2320  O   VAL  304      12.899  72.596  26.861  1.00 48.95
ATOM   2321  N   ASP  305      14.297  71.946  25.212  1.00 48.52
ATOM   2322  CA  ASP  305      14.143  73.165  24.432  1.00 48.31
ATOM   2323  CB  ASP  305      14.968  73.067  23.143  1.00 49.45
ATOM   2324  CG  ASP  305      16.441  72.715  23.412  1.00 51.00
ATOM   2325  OD1 ASP  305      17.056  73.323  24.317  1.00 50.99
ATOM   2326  OD2 ASP  305      16.994  71.834  22.715  1.00 51.84
ATOM   2327  C   ASP  305      12.677  73.460  24.122  1.00 47.77
ATOM   2328  O   ASP  305      12.341  74.541  23.641  1.00 48.22
ATOM   2329  N   GLU  306      11.799  72.505  24.407  1.00 46.84
ATOM   2330  CA  GLU  306      10.378  72.713  24.176  1.00 46.34
ATOM   2331  CB  GLU  306       9.831  71.683  23.184  1.00 46.20
ATOM   2332  CG  GLU  306       9.866  72.216  21.761  1.00 48.15
ATOM   2333  CD  GLU  306       9.571  71.175  20.692  1.00 49.26
ATOM   2334  OE1 GLU  306       8.514  70.499  20.768  1.00 50.03
ATOM   2335  OE2 GLU  306      10.398  71.049  19.759  1.00 49.62
ATOM   2336  C   GLU  306       9.635  72.661  25.493  1.00 45.99
ATOM   2337  O   GLU  306       8.459  72.331  25.550  1.00 45.90
ATOM   2338  N   ASN  307      10.350  72.997  26.560  1.00 46.00
ATOM   2339  CA  ASN  307       9.787  73.029  27.902  1.00 45.60
ATOM   2340  CB  ASN  307       9.033  74.342  28.094  1.00 46.42
ATOM   2341  CG  ASN  307       9.971  75.531  28.224  1.00 46.98
ATOM   2342  OD1 ASN  307      10.435  75.849  29.321  1.00 47.63
ATOM   2343  ND2 ASN  307      10.273  76.181  27.102  1.00 46.93
ATOM   2344  C   ASN  307       8.886  71.853  28.246  1.00 45.05
ATOM   2345  O   ASN  307       7.812  72.029  28.829  1.00 45.19
ATOM   2346  N   LEU  308       9.336  70.650  27.900  1.00 44.24
ATOM   2347  CA  LEU  308       8.575  69.439  28.180  1.00 43.28
ATOM   2348  CB  LEU  308       8.376  68.637  26.893  1.00 43.27
ATOM   2349  CG  LEU  308       7.070  68.825  26.115  1.00 44.09
ATOM   2350  CD1 LEU  308       6.765  70.294  25.935  1.00 44.22
ATOM   2351  CD2 LEU  308       7.182  68.139  24.760  1.00 43.94
ATOM   2352  C   LEU  308       9.287  68.570  29.205  1.00 42.96
ATOM   2353  O   LEU  308       8.688  67.660  29.775  1.00 42.27
ATOM   2354  N   LEU  309      10.560  68.868  29.448  1.00 43.49
ATOM   2355  CA  LEU  309      11.368  68.077  30.371  1.00 44.85
```

Figure 4

```
ATOM   2356  CB  LEU   309      12.030  66.936  29.581  1.00 43.53
ATOM   2357  CG  LEU   309      12.958  65.925  30.254  1.00 42.07
ATOM   2358  CD1 LEU   309      12.235  65.226  31.390  1.00 40.83
ATOM   2359  CD2 LEU   309      13.416  64.913  29.212  1.00 42.11
ATOM   2360  C   LEU   309      12.436  68.900  31.108  1.00 46.21
ATOM   2361  O   LEU   309      13.074  69.777  30.518  1.00 46.04
ATOM   2362  N   PHE   310      12.625  68.601  32.397  1.00 47.92
ATOM   2363  CA  PHE   310      13.608  69.293  33.238  1.00 49.25
ATOM   2364  CB  PHE   310      15.013  69.093  32.666  1.00 48.20
ATOM   2365  CG  PHE   310      15.438  67.650  32.590  1.00 47.06
ATOM   2366  CD1 PHE   310      16.338  67.228  31.615  1.00 46.24
ATOM   2367  CD2 PHE   310      14.947  66.715  33.497  1.00 46.63
ATOM   2368  CE1 PHE   310      16.740  65.903  31.540  1.00 45.74
ATOM   2369  CE2 PHE   310      15.344  65.385  33.433  1.00 46.27
ATOM   2370  CZ  PHE   310      16.243  64.978  32.451  1.00 45.93
ATOM   2371  C   PHE   310      13.292  70.785  33.345  1.00 51.16
ATOM   2372  O   PHE   310      14.185  71.616  33.561  1.00 50.84
ATOM   2373  N   HIS   311      12.009  71.109  33.183  1.00 53.40
ATOM   2374  CA  HIS   311      11.529  72.482  33.262  1.00 55.80
ATOM   2375  CB  HIS   311      11.744  73.012  34.683  1.00 57.57
ATOM   2376  CG  HIS   311      11.212  72.098  35.745  1.00 59.78
ATOM   2377  CD2 HIS   311      11.848  71.363  36.689  1.00 60.29
ATOM   2378  ND1 HIS   311       9.867  71.815  35.879  1.00 60.36
ATOM   2379  CE1 HIS   311       9.699  70.944  36.860  1.00 60.99
ATOM   2380  NE2 HIS   311      10.885  70.654  37.368  1.00 60.85
ATOM   2381  C   HIS   311      12.214  73.384  32.236  1.00 56.24
ATOM   2382  O   HIS   311      12.288  74.608  32.415  1.00 56.87
ATOM   2383  N   GLY   312      12.705  72.772  31.159  1.00 55.96
ATOM   2384  CA  GLY   312      13.366  73.522  30.109  1.00 55.87
ATOM   2385  C   GLY   312      14.820  73.804  30.420  1.00 56.16
ATOM   2386  O   GLY   312      15.563  74.264  29.562  1.00 56.58
ATOM   2387  N   GLU   313      15.235  73.519  31.646  1.00 56.52
ATOM   2388  CA  GLU   313      16.612  73.765  32.048  1.00 57.69
ATOM   2389  CB  GLU   313      16.621  74.379  33.447  1.00 59.84
ATOM   2390  CG  GLU   313      15.849  75.698  33.515  1.00 63.16
ATOM   2391  CD  GLU   313      15.388  76.061  34.925  1.00 65.16
ATOM   2392  OE1 GLU   313      14.554  75.315  35.503  1.00 66.01
ATOM   2393  OE2 GLU   313      15.858  77.096  35.455  1.00 66.34
ATOM   2394  C   GLU   313      17.439  72.484  32.011  1.00 57.06
ATOM   2395  O   GLU   313      17.155  71.529  32.728  1.00 57.01
ATOM   2396  N   ALA   314      18.463  72.472  31.169  1.00 56.56
ATOM   2397  CA  ALA   314      19.316  71.305  31.029  1.00 56.76
ATOM   2398  CB  ALA   314      19.454  70.939  29.557  1.00 56.47
ATOM   2399  C   ALA   314      20.699  71.490  31.643  1.00 56.94
ATOM   2400  O   ALA   314      21.310  72.558  31.527  1.00 57.46
ATOM   2401  N   SER   315      21.183  70.422  32.276  1.00 56.73
ATOM   2402  CA  SER   315      22.487  70.383  32.932  1.00 56.15
ATOM   2403  CB  SER   315      22.666  69.029  33.624  1.00 56.44
ATOM   2404  OG  SER   315      23.981  68.868  34.130  1.00 57.39
ATOM   2405  C   SER   315      23.673  70.627  32.003  1.00 56.00
ATOM   2406  O   SER   315      23.595  70.416  30.793  1.00 55.42
ATOM   2407  N   GLU   316      24.776  71.070  32.598  1.00 56.67
ATOM   2408  CA  GLU   316      26.012  71.346  31.875  1.00 57.46
ATOM   2409  CB  GLU   316      27.111  71.754  32.860  1.00 58.71
ATOM   2410  CG  GLU   316      28.458  72.050  32.206  1.00 60.34
ATOM   2411  CD  GLU   316      28.442  73.343  31.406  1.00 61.64
ATOM   2412  OE1 GLU   316      28.288  74.420  32.031  1.00 62.41
ATOM   2413  OE2 GLU   316      28.574  73.280  30.160  1.00 61.76
ATOM   2414  C   GLU   316      26.442  70.078  31.161  1.00 57.35
```

Figure 4

ATOM	2415	O	GLU	316	26.770	70.088	29.972	1.00	57.68
ATOM	2416	N	GLN	317	26.439	68.988	31.920	1.00	56.84
ATOM	2417	CA	GLN	317	26.817	67.677	31.427	1.00	56.23
ATOM	2418	CB	GLN	317	26.760	66.669	32.580	1.00	55.93
ATOM	2419	CG	GLN	317	27.504	67.113	33.840	1.00	55.46
ATOM	2420	CD	GLN	317	27.063	66.355	35.085	1.00	55.01
ATOM	2421	OE1	GLN	317	27.246	65.140	35.194	1.00	54.83
ATOM	2422	NE2	GLN	317	26.468	67.074	36.029	1.00	54.68
ATOM	2423	C	GLN	317	25.902	67.210	30.290	1.00	56.37
ATOM	2424	O	GLN	317	26.376	66.634	29.312	1.00	56.16
ATOM	2425	N	LEU	318	24.599	67.476	30.412	1.00	56.41
ATOM	2426	CA	LEU	318	23.616	67.043	29.413	1.00	56.48
ATOM	2427	CB	LEU	318	22.190	67.333	29.890	1.00	55.59
ATOM	2428	CG	LEU	318	21.084	66.700	29.034	1.00	54.71
ATOM	2429	CD1	LEU	318	21.090	65.191	29.231	1.00	53.88
ATOM	2430	CD2	LEU	318	19.731	67.268	29.422	1.00	54.28
ATOM	2431	C	LEU	318	23.784	67.621	28.017	1.00	56.99
ATOM	2432	O	LEU	318	23.692	66.893	27.029	1.00	57.21
ATOM	2433	N	ARG	319	24.011	68.924	27.919	1.00	57.16
ATOM	2434	CA	ARG	319	24.177	69.530	26.606	1.00	57.68
ATOM	2435	CB	ARG	319	23.870	71.026	26.690	1.00	59.32
ATOM	2436	CG	ARG	319	22.420	71.284	27.105	1.00	62.20
ATOM	2437	CD	ARG	319	22.125	72.743	27.401	1.00	64.53
ATOM	2438	NE	ARG	319	20.758	72.927	27.892	1.00	66.89
ATOM	2439	CZ	ARG	319	20.297	74.055	28.433	1.00	68.29
ATOM	2440	NH1	ARG	319	21.096	75.112	28.555	1.00	68.30
ATOM	2441	NH2	ARG	319	19.034	74.127	28.851	1.00	68.25
ATOM	2442	C	ARG	319	25.587	69.278	26.081	1.00	57.09
ATOM	2443	O	ARG	319	26.049	69.951	25.160	1.00	57.05
ATOM	2444	N	THR	320	26.246	68.277	26.667	1.00	56.25
ATOM	2445	CA	THR	320	27.612	67.888	26.318	1.00	55.15
ATOM	2446	CB	THR	320	28.478	67.836	27.589	1.00	54.85
ATOM	2447	OG1	THR	320	28.601	69.158	28.133	1.00	54.94
ATOM	2448	CG2	THR	320	29.854	67.262	27.287	1.00	54.63
ATOM	2449	C	THR	320	27.689	66.524	25.613	1.00	55.04
ATOM	2450	O	THR	320	27.476	65.480	26.229	1.00	55.13
ATOM	2451	N	ARG	321	28.017	66.536	24.326	1.00	54.38
ATOM	2452	CA	ARG	321	28.106	65.304	23.545	1.00	54.36
ATOM	2453	CB	ARG	321	28.841	65.586	22.236	1.00	56.05
ATOM	2454	CG	ARG	321	28.153	66.651	21.402	1.00	59.03
ATOM	2455	CD	ARG	321	28.943	67.013	20.156	1.00	61.60
ATOM	2456	NE	ARG	321	28.331	68.123	19.426	1.00	63.68
ATOM	2457	CZ	ARG	321	28.909	68.753	18.406	1.00	65.43
ATOM	2458	NH1	ARG	321	30.119	68.381	17.997	1.00	65.83
ATOM	2459	NH2	ARG	321	28.280	69.750	17.792	1.00	65.76
ATOM	2460	C	ARG	321	28.765	64.123	24.262	1.00	52.97
ATOM	2461	O	ARG	321	29.885	64.234	24.758	1.00	53.13
ATOM	2462	N	GLY	322	28.056	62.996	24.316	1.00	51.39
ATOM	2463	CA	GLY	322	28.592	61.802	24.950	1.00	49.22
ATOM	2464	C	GLY	322	28.198	61.609	26.402	1.00	48.17
ATOM	2465	O	GLY	322	28.450	60.550	26.986	1.00	48.17
ATOM	2466	N	ALA	323	27.574	62.627	26.988	1.00	46.66
ATOM	2467	CA	ALA	323	27.150	62.573	28.385	1.00	44.99
ATOM	2468	CB	ALA	323	26.462	63.861	28.761	1.00	45.87
ATOM	2469	C	ALA	323	26.224	61.403	28.676	1.00	43.43
ATOM	2470	O	ALA	323	26.514	60.562	29.530	1.00	43.02
ATOM	2471	N	PHE	324	25.094	61.361	27.981	1.00	41.61
ATOM	2472	CA	PHE	324	24.147	60.282	28.185	1.00	40.44
ATOM	2473	CB	PHE	324	22.797	60.631	27.564	1.00	38.94

```
ATOM   2474  CG  PHE  324      21.644  59.988  28.262  1.00 38.08
ATOM   2475  CD1 PHE  324      21.047  60.613  29.360  1.00 37.48
ATOM   2476  CD2 PHE  324      21.185  58.733  27.860  1.00 36.96
ATOM   2477  CE1 PHE  324      20.010  59.998  30.050  1.00 37.11
ATOM   2478  CE2 PHE  324      20.146  58.105  28.542  1.00 37.79
ATOM   2479  CZ  PHE  324      19.555  58.739  29.643  1.00 37.73
ATOM   2480  C   PHE  324      24.721  59.033  27.525  1.00 40.11
ATOM   2481  O   PHE  324      24.785  58.937  26.289  1.00 40.76
ATOM   2482  N   GLU  325      25.129  58.072  28.350  1.00 39.06
ATOM   2483  CA  GLU  325      25.740  56.851  27.844  1.00 37.85
ATOM   2484  CB  GLU  325      26.846  56.418  28.781  1.00 38.17
ATOM   2485  CG  GLU  325      27.790  57.528  29.085  1.00 40.68
ATOM   2486  CD  GLU  325      28.922  57.075  29.951  1.00 42.47
ATOM   2487  OE1 GLU  325      28.653  56.608  31.086  1.00 44.06
ATOM   2488  OE2 GLU  325      30.080  57.181  29.490  1.00 44.51
ATOM   2489  C   GLU  325      24.799  55.693  27.641  1.00 36.60
ATOM   2490  O   GLU  325      23.903  55.445  28.447  1.00 37.31
ATOM   2491  N   THR  326      25.019  54.968  26.554  1.00 35.30
ATOM   2492  CA  THR  326      24.193  53.816  26.245  1.00 33.37
ATOM   2493  CB  THR  326      24.875  52.921  25.207  1.00 31.58
ATOM   2494  OG1 THR  326      24.934  53.617  23.956  1.00 29.82
ATOM   2495  CG2 THR  326      24.113  51.619  25.041  1.00 29.94
ATOM   2496  C   THR  326      23.951  53.016  27.515  1.00 33.05
ATOM   2497  O   THR  326      22.846  52.528  27.742  1.00 33.99
ATOM   2498  N   ARG  327      24.981  52.902  28.349  1.00 32.29
ATOM   2499  CA  ARG  327      24.859  52.148  29.588  1.00 31.76
ATOM   2500  CB  ARG  327      26.146  52.245  30.417  1.00 33.30
ATOM   2501  CG  ARG  327      26.226  51.162  31.485  1.00 36.71
ATOM   2502  CD  ARG  327      27.596  51.043  32.177  1.00 38.88
ATOM   2503  NE  ARG  327      27.795  52.024  33.249  1.00 40.62
ATOM   2504  CZ  ARG  327      28.274  53.255  33.069  1.00 41.13
ATOM   2505  NH1 ARG  327      28.615  53.670  31.846  1.00 40.49
ATOM   2506  NH2 ARG  327      28.393  54.078  34.113  1.00 40.82
ATOM   2507  C   ARG  327      23.681  52.691  30.387  1.00 30.62
ATOM   2508  O   ARG  327      22.888  51.930  30.940  1.00 29.96
ATOM   2509  N   PHE  328      23.559  54.014  30.425  1.00 29.60
ATOM   2510  CA  PHE  328      22.479  54.660  31.154  1.00 28.70
ATOM   2511  CB  PHE  328      22.632  56.176  31.069  1.00 28.03
ATOM   2512  CG  PHE  328      23.903  56.684  31.686  1.00 27.73
ATOM   2513  CD1 PHE  328      24.337  57.975  31.439  1.00 27.37
ATOM   2514  CD2 PHE  328      24.678  55.857  32.505  1.00 28.92
ATOM   2515  CE1 PHE  328      25.526  58.437  31.992  1.00 28.75
ATOM   2516  CE2 PHE  328      25.871  56.305  33.069  1.00 28.74
ATOM   2517  CZ  PHE  328      26.298  57.599  32.812  1.00 28.68
ATOM   2518  C   PHE  328      21.135  54.226  30.590  1.00 29.06
ATOM   2519  O   PHE  328      20.189  53.953  31.351  1.00 29.59
ATOM   2520  N   VAL  329      21.057  54.154  29.257  1.00 28.40
ATOM   2521  CA  VAL  329      19.830  53.735  28.587  1.00 26.44
ATOM   2522  CB  VAL  329      20.040  53.552  27.059  1.00 25.14
ATOM   2523  CG1 VAL  329      18.737  53.107  26.387  1.00 22.55
ATOM   2524  CG2 VAL  329      20.542  54.841  26.444  1.00 23.05
ATOM   2525  C   VAL  329      19.388  52.399  29.166  1.00 27.98
ATOM   2526  O   VAL  329      18.240  52.239  29.576  1.00 27.88
ATOM   2527  N   SER  330      20.308  51.442  29.219  1.00 28.76
ATOM   2528  CA  SER  330      19.966  50.117  29.718  1.00 30.08
ATOM   2529  CB  SER  330      21.136  49.171  29.534  1.00 30.45
ATOM   2530  OG  SER  330      20.720  47.852  29.822  1.00 31.92
ATOM   2531  C   SER  330      19.534  50.107  31.172  1.00 31.40
ATOM   2532  O   SER  330      18.690  49.298  31.577  1.00 31.74
```

Figure 4

ATOM	2533	N	GLN	331	20.118	50.993	31.972	1.00	32.45
ATOM	2534	CA	GLN	331	19.745	51.061	33.381	1.00	33.16
ATOM	2535	CB	GLN	331	20.668	51.992	34.151	1.00	33.58
ATOM	2536	CG	GLN	331	22.093	51.540	34.194	1.00	35.83
ATOM	2537	CD	GLN	331	22.947	52.534	34.919	1.00	37.72
ATOM	2538	OE1	GLN	331	22.626	52.927	36.043	1.00	39.62
ATOM	2539	NE2	GLN	331	24.042	52.958	34.291	1.00	38.98
ATOM	2540	C	GLN	331	18.327	51.591	33.482	1.00	33.78
ATOM	2541	O	GLN	331	17.428	50.881	33.938	1.00	34.06
ATOM	2542	N	VAL	332	18.129	52.835	33.038	1.00	33.77
ATOM	2543	CA	VAL	332	16.808	53.457	33.097	1.00	33.65
ATOM	2544	CB	VAL	332	16.760	54.791	32.282	1.00	32.19
ATOM	2545	CG1	VAL	332	17.279	54.584	30.905	1.00	33.04
ATOM	2546	CG2	VAL	332	15.340	55.312	32.215	1.00	31.67
ATOM	2547	C	VAL	332	15.695	52.505	32.638	1.00	34.20
ATOM	2548	O	VAL	332	14.571	52.566	33.139	1.00	34.51
ATOM	2549	N	GLU	333	16.001	51.607	31.711	1.00	34.30
ATOM	2550	CA	GLU	333	14.981	50.676	31.258	1.00	34.92
ATOM	2551	CB	GLU	333	15.210	50.289	29.795	1.00	34.40
ATOM	2552	CG	GLU	333	14.893	51.413	28.837	1.00	33.07
ATOM	2553	CD	GLU	333	14.806	50.956	27.409	1.00	31.80
ATOM	2554	OE1	GLU	333	13.983	50.060	27.114	1.00	31.65
ATOM	2555	OE2	GLU	333	15.561	51.504	26.581	1.00	31.72
ATOM	2556	C	GLU	333	14.949	49.438	32.135	1.00	35.76
ATOM	2557	O	GLU	333	14.163	48.520	31.911	1.00	35.73
ATOM	2558	N	SER	334	15.814	49.419	33.138	1.00	36.91
ATOM	2559	CA	SER	334	15.876	48.307	34.071	1.00	38.13
ATOM	2560	CB	SER	334	17.328	47.934	34.346	1.00	39.38
ATOM	2561	OG	SER	334	17.460	46.524	34.468	1.00	41.52
ATOM	2562	C	SER	334	15.201	48.747	35.362	1.00	37.93
ATOM	2563	O	SER	334	15.053	47.973	36.306	1.00	38.63
ATOM	2564	N	ASP	335	14.807	50.014	35.385	1.00	38.51
ATOM	2565	CA	ASP	335	14.133	50.619	36.521	1.00	38.59
ATOM	2566	CB	ASP	335	13.776	52.061	36.173	1.00	39.10
ATOM	2567	CG	ASP	335	13.346	52.864	37.373	1.00	39.89
ATOM	2568	OD1	ASP	335	12.278	52.547	37.950	1.00	40.30
ATOM	2569	OD2	ASP	335	14.079	53.816	37.737	1.00	39.90
ATOM	2570	C	ASP	335	12.876	49.809	36.840	1.00	39.11
ATOM	2571	O	ASP	335	12.241	49.249	35.945	1.00	39.03
ATOM	2572	N	THR	336	12.517	49.768	38.119	1.00	39.68
ATOM	2573	CA	THR	336	11.372	48.999	38.605	1.00	39.94
ATOM	2574	CB	THR	336	11.773	48.297	39.896	1.00	39.68
ATOM	2575	OG1	THR	336	12.901	47.464	39.630	1.00	40.95
ATOM	2576	CG2	THR	336	10.650	47.452	40.426	1.00	39.84
ATOM	2577	C	THR	336	10.043	49.735	38.853	1.00	40.52
ATOM	2578	O	THR	336	8.984	49.108	38.931	1.00	40.91
ATOM	2579	N	GLY	337	10.085	51.054	38.970	1.00	40.80
ATOM	2580	CA	GLY	337	8.870	51.804	39.234	1.00	41.83
ATOM	2581	C	GLY	337	9.307	52.948	40.112	1.00	42.60
ATOM	2582	O	GLY	337	8.990	54.105	39.865	1.00	43.33
ATOM	2583	N	ASP	338	10.043	52.604	41.156	1.00	43.47
ATOM	2584	CA	ASP	338	10.606	53.589	42.059	1.00	44.40
ATOM	2585	CB	ASP	338	11.354	52.868	43.175	1.00	44.83
ATOM	2586	CG	ASP	338	12.303	51.808	42.637	1.00	45.34
ATOM	2587	OD1	ASP	338	11.879	51.032	41.751	1.00	46.12
ATOM	2588	OD2	ASP	338	13.465	51.742	43.087	1.00	45.59
ATOM	2589	C	ASP	338	11.597	54.296	41.142	1.00	44.84
ATOM	2590	O	ASP	338	12.605	53.709	40.756	1.00	45.53
ATOM	2591	N	ARG	339	11.310	55.533	40.763	1.00	44.81

Figure 4

```
ATOM   2592  CA  ARG  339      12.208  56.256  39.874  1.00 45.11
ATOM   2593  CB  ARG  339      11.702  57.687  39.654  1.00 45.72
ATOM   2594  CG  ARG  339      10.466  57.799  38.783  1.00 46.11
ATOM   2595  CD  ARG  339       9.201  57.413  39.521  1.00 46.99
ATOM   2596  NE  ARG  339       8.041  57.492  38.633  1.00 47.58
ATOM   2597  CZ  ARG  339       6.780  57.326  39.017  1.00 47.30
ATOM   2598  NH1 ARG  339       6.492  57.068  40.287  1.00 47.38
ATOM   2599  NH2 ARG  339       5.806  57.413  38.123  1.00 47.44
ATOM   2600  C   ARG  339      13.637  56.295  40.419  1.00 44.98
ATOM   2601  O   ARG  339      14.466  57.084  39.960  1.00 44.83
ATOM   2602  N   LYS  340      13.922  55.441  41.394  1.00 44.75
ATOM   2603  CA  LYS  340      15.238  55.394  42.001  1.00 45.05
ATOM   2604  CB  LYS  340      15.341  54.179  42.917  1.00 46.19
ATOM   2605  CG  LYS  340      14.358  54.250  44.081  1.00 47.87
ATOM   2606  CD  LYS  340      14.598  53.154  45.094  1.00 49.25
ATOM   2607  CE  LYS  340      13.365  52.949  45.957  1.00 50.44
ATOM   2608  NZ  LYS  340      13.353  51.589  46.598  1.00 51.78
ATOM   2609  C   LYS  340      16.398  55.422  41.014  1.00 44.66
ATOM   2610  O   LYS  340      17.186  56.372  41.026  1.00 44.90
ATOM   2611  N   GLN  341      16.509  54.408  40.155  1.00 43.94
ATOM   2612  CA  GLN  341      17.603  54.362  39.174  1.00 42.93
ATOM   2613  CB  GLN  341      17.598  53.028  38.435  1.00 45.04
ATOM   2614  CG  GLN  341      18.035  51.860  39.289  1.00 48.03
ATOM   2615  CD  GLN  341      18.758  50.801  38.482  1.00 49.69
ATOM   2616  OE1 GLN  341      19.731  51.101  37.779  1.00 50.67
ATOM   2617  NE2 GLN  341      18.297  49.556  38.581  1.00 50.43
ATOM   2618  C   GLN  341      17.616  55.497  38.146  1.00 40.93
ATOM   2619  O   GLN  341      18.672  56.057  37.839  1.00 38.85
ATOM   2620  N   ILE  342      16.449  55.824  37.600  1.00 39.61
ATOM   2621  CA  ILE  342      16.364  56.905  36.624  1.00 39.07
ATOM   2622  CB  ILE  342      14.920  57.110  36.130  1.00 39.24
ATOM   2623  CG2 ILE  342      14.880  58.226  35.107  1.00 39.19
ATOM   2624  CG1 ILE  342      14.392  55.817  35.501  1.00 39.87
ATOM   2625  CD1 ILE  342      12.945  55.902  35.070  1.00 40.76
ATOM   2626  C   ILE  342      16.832  58.185  37.301  1.00 38.43
ATOM   2627  O   ILE  342      17.704  58.892  36.795  1.00 37.48
ATOM   2628  N   TYR  343      16.240  58.466  38.456  1.00 38.93
ATOM   2629  CA  TYR  343      16.580  59.647  39.236  1.00 39.71
ATOM   2630  CB  TYR  343      15.813  59.656  40.567  1.00 40.97
ATOM   2631  CG  TYR  343      16.173  60.835  41.448  1.00 42.53
ATOM   2632  CD1 TYR  343      15.344  61.954  41.521  1.00 43.30
ATOM   2633  CE1 TYR  343      15.730  63.092  42.228  1.00 44.58
ATOM   2634  CD2 TYR  343      17.397  60.880  42.119  1.00 43.04
ATOM   2635  CE2 TYR  343      17.791  62.014  42.826  1.00 43.55
ATOM   2636  CZ  TYR  343      16.958  63.117  42.872  1.00 44.31
ATOM   2637  OH  TYR  343      17.369  64.260  43.523  1.00 45.74
ATOM   2638  C   TYR  343      18.070  59.635  39.532  1.00 39.93
ATOM   2639  O   TYR  343      18.789  60.598  39.262  1.00 40.28
ATOM   2640  N   ASN  344      18.525  58.529  40.098  1.00 40.14
ATOM   2641  CA  ASN  344      19.924  58.371  40.460  1.00 40.97
ATOM   2642  CB  ASN  344      20.146  56.958  40.989  1.00 42.94
ATOM   2643  CG  ASN  344      21.287  56.880  41.977  1.00 44.68
ATOM   2644  OD1 ASN  344      22.448  57.137  41.628  1.00 46.05
ATOM   2645  ND2 ASN  344      20.965  56.531  43.225  1.00 44.93
ATOM   2646  C   ASN  344      20.869  58.649  39.292  1.00 40.46
ATOM   2647  O   ASN  344      21.946  59.208  39.483  1.00 40.33
ATOM   2648  N   ILE  345      20.460  58.262  38.085  1.00 40.50
ATOM   2649  CA  ILE  345      21.280  58.467  36.890  1.00 39.89
ATOM   2650  CB  ILE  345      20.803  57.555  35.720  1.00 39.76
```

```
ATOM   2651  CG2 ILE   345      21.597  57.849  34.448  1.00 38.62
ATOM   2652  CG1 ILE   345      20.966  56.090  36.114  1.00 38.74
ATOM   2653  CD1 ILE   345      20.201  55.151  35.242  1.00 38.61
ATOM   2654  C   ILE   345      21.247  59.924  36.434  1.00 39.80
ATOM   2655  O   ILE   345      22.281  60.490  36.074  1.00 39.67
ATOM   2656  N   LEU   346      20.062  60.529  36.449  1.00 39.59
ATOM   2657  CA  LEU   346      19.912  61.923  36.029  1.00 39.58
ATOM   2658  CB  LEU   346      18.434  62.255  35.818  1.00 37.79
ATOM   2659  CG  LEU   346      17.809  61.528  34.625  1.00 36.58
ATOM   2660  CD1 LEU   346      16.277  61.599  34.684  1.00 35.18
ATOM   2661  CD2 LEU   346      18.363  62.145  33.337  1.00 35.05
ATOM   2662  C   LEU   346      20.519  62.892  37.034  1.00 40.82
ATOM   2663  O   LEU   346      21.177  63.857  36.654  1.00 41.02
ATOM   2664  N   SER   347      20.298  62.646  38.322  1.00 42.34
ATOM   2665  CA  SER   347      20.859  63.530  39.339  1.00 43.44
ATOM   2666  CB  SER   347      20.491  63.042  40.745  1.00 43.90
ATOM   2667  OG  SER   347      20.665  61.639  40.868  1.00 45.32
ATOM   2668  C   SER   347      22.368  63.556  39.156  1.00 43.44
ATOM   2669  O   SER   347      22.974  64.624  39.051  1.00 44.11
ATOM   2670  N   THR   348      22.969  62.374  39.096  1.00 43.10
ATOM   2671  CA  THR   348      24.407  62.285  38.909  1.00 42.97
ATOM   2672  CB  THR   348      24.853  60.830  38.700  1.00 42.31
ATOM   2673  OG1 THR   348      24.666  60.096  39.918  1.00 42.08
ATOM   2674  CG2 THR   348      26.322  60.780  38.282  1.00 40.85
ATOM   2675  C   THR   348      24.798  63.093  37.683  1.00 43.25
ATOM   2676  O   THR   348      25.796  63.813  37.680  1.00 43.52
ATOM   2677  N   LEU   349      23.990  62.982  36.640  1.00 43.57
ATOM   2678  CA  LEU   349      24.271  63.697  35.412  1.00 44.17
ATOM   2679  CB  LEU   349      23.343  63.180  34.311  1.00 44.43
ATOM   2680  CG  LEU   349      23.787  63.204  32.847  1.00 44.86
ATOM   2681  CD1 LEU   349      25.198  62.658  32.688  1.00 44.59
ATOM   2682  CD2 LEU   349      22.790  62.375  32.046  1.00 44.64
ATOM   2683  C   LEU   349      24.102  65.201  35.638  1.00 44.32
ATOM   2684  O   LEU   349      24.317  66.003  34.726  1.00 45.33
ATOM   2685  N   GLY   350      23.722  65.574  36.862  1.00 43.94
ATOM   2686  CA  GLY   350      23.559  66.981  37.210  1.00 43.15
ATOM   2687  C   GLY   350      22.167  67.570  37.038  1.00 42.49
ATOM   2688  O   GLY   350      22.024  68.752  36.703  1.00 41.70
ATOM   2689  N   LEU   351      21.143  66.758  37.288  1.00 41.97
ATOM   2690  CA  LEU   351      19.758  67.197  37.132  1.00 41.45
ATOM   2691  CB  LEU   351      19.194  66.676  35.812  1.00 40.99
ATOM   2692  CG  LEU   351      19.875  67.115  34.522  1.00 40.66
ATOM   2693  CD1 LEU   351      19.516  66.144  33.416  1.00 41.63
ATOM   2694  CD2 LEU   351      19.453  68.533  34.172  1.00 40.77
ATOM   2695  C   LEU   351      18.858  66.718  38.262  1.00 41.15
ATOM   2696  O   LEU   351      19.170  65.760  38.973  1.00 40.88
ATOM   2697  N   ARG   352      17.720  67.379  38.410  1.00 41.10
ATOM   2698  CA  ARG   352      16.782  67.007  39.457  1.00 41.25
ATOM   2699  CB  ARG   352      16.614  68.173  40.431  1.00 42.65
ATOM   2700  CG  ARG   352      17.929  68.581  41.070  1.00 43.68
ATOM   2701  CD  ARG   352      18.504  67.421  41.851  1.00 45.59
ATOM   2702  NE  ARG   352      19.960  67.478  41.917  1.00 47.73
ATOM   2703  CZ  ARG   352      20.715  66.567  42.521  1.00 48.77
ATOM   2704  NH1 ARG   352      20.143  65.524  43.119  1.00 49.05
ATOM   2705  NH2 ARG   352      22.038  66.700  42.519  1.00 49.14
ATOM   2706  C   ARG   352      15.458  66.621  38.827  1.00 39.59
ATOM   2707  O   ARG   352      14.512  67.399  38.793  1.00 40.34
ATOM   2708  N   PRO   353      15.378  65.388  38.324  1.00 38.06
ATOM   2709  CD  PRO   353      16.325  64.285  38.555  1.00 37.28
```

Figure 4


```
ATOM   2710  CA  PRO  353      14.159  64.901  37.683  1.00 37.45
ATOM   2711  CB  PRO  353      14.595  63.552  37.134  1.00 37.27
ATOM   2712  CG  PRO  353      15.491  63.064  38.232  1.00 36.92
ATOM   2713  C   PRO  353      12.998  64.763  38.650  1.00 36.35
ATOM   2714  O   PRO  353      13.180  64.360  39.791  1.00 36.28
ATOM   2715  N   SER  354      11.805  65.110  38.194  1.00 35.82
ATOM   2716  CA  SER  354      10.625  64.951  39.028  1.00 36.40
ATOM   2717  CB  SER  354       9.570  66.010  38.698  1.00 35.94
ATOM   2718  OG  SER  354       8.944  65.725  37.459  1.00 35.63
ATOM   2719  C   SER  354      10.091  63.570  38.653  1.00 36.41
ATOM   2720  O   SER  354      10.592  62.948  37.716  1.00 37.42
ATOM   2721  N   THR  355       9.087  63.091  39.375  1.00 36.02
ATOM   2722  CA  THR  355       8.493  61.790  39.099  1.00 35.68
ATOM   2723  CB  THR  355       7.200  61.615  39.923  1.00 36.38
ATOM   2724  OG1 THR  355       7.525  61.645  41.316  1.00 37.75
ATOM   2725  CG2 THR  355       6.510  60.293  39.598  1.00 36.44
ATOM   2726  C   THR  355       8.161  61.633  37.609  1.00 35.80
ATOM   2727  O   THR  355       8.319  60.548  37.029  1.00 34.73
ATOM   2728  N   THR  356       7.698  62.720  36.994  1.00 35.28
ATOM   2729  CA  THR  356       7.336  62.690  35.586  1.00 35.39
ATOM   2730  CB  THR  356       6.287  63.774  35.263  1.00 35.59
ATOM   2731  OG1 THR  356       6.651  64.990  35.925  1.00 35.39
ATOM   2732  CG2 THR  356       4.892  63.331  35.719  1.00 34.33
ATOM   2733  C   THR  356       8.542  62.848  34.662  1.00 35.30
ATOM   2734  O   THR  356       8.560  62.285  33.559  1.00 34.91
ATOM   2735  N   ASP  357       9.537  63.624  35.089  1.00 35.07
ATOM   2736  CA  ASP  357      10.740  63.782  34.277  1.00 35.80
ATOM   2737  CB  ASP  357      11.804  64.598  35.012  1.00 36.76
ATOM   2738  CG  ASP  357      11.451  66.077  35.116  1.00 38.19
ATOM   2739  OD1 ASP  357      11.475  66.778  34.071  1.00 37.60
ATOM   2740  OD2 ASP  357      11.158  66.538  36.249  1.00 38.76
ATOM   2741  C   ASP  357      11.277  62.373  34.039  1.00 35.97
ATOM   2742  O   ASP  357      11.460  61.942  32.901  1.00 36.94
ATOM   2743  N   CYS  358      11.498  61.649  35.131  1.00 35.67
ATOM   2744  CA  CYS  358      12.013  60.293  35.057  1.00 35.44
ATOM   2745  CB  CYS  358      12.051  59.658  36.447  1.00 35.93
ATOM   2746  SG  CYS  358      13.247  60.410  37.575  1.00 35.81
ATOM   2747  C   CYS  358      11.177  59.433  34.138  1.00 34.88
ATOM   2748  O   CYS  358      11.711  58.698  33.308  1.00 35.87
ATOM   2749  N   ASP  359       9.863  59.517  34.290  1.00 34.10
ATOM   2750  CA  ASP  359       8.960  58.729  33.464  1.00 33.10
ATOM   2751  CB  ASP  359       7.519  58.964  33.910  1.00 35.03
ATOM   2752  CG  ASP  359       7.118  58.058  35.062  1.00 36.65
ATOM   2753  OD1 ASP  359       7.950  57.850  35.975  1.00 38.15
ATOM   2754  OD2 ASP  359       5.969  57.561  35.055  1.00 37.12
ATOM   2755  C   ASP  359       9.130  59.058  31.985  1.00 31.16
ATOM   2756  O   ASP  359       9.090  58.170  31.133  1.00 30.01
ATOM   2757  N   ILE  360       9.325  60.334  31.682  1.00 29.54
ATOM   2758  CA  ILE  360       9.524  60.741  30.300  1.00 28.61
ATOM   2759  CB  ILE  360       9.546  62.273  30.162  1.00 27.75
ATOM   2760  CG2 ILE  360      10.255  62.668  28.874  1.00 27.01
ATOM   2761  CG1 ILE  360       8.112  62.818  30.235  1.00 26.18
ATOM   2762  CD1 ILE  360       8.024  64.322  30.190  1.00 23.23
ATOM   2763  C   ILE  360      10.857  60.176  29.825  1.00 29.21
ATOM   2764  O   ILE  360      10.919  59.480  28.805  1.00 29.88
ATOM   2765  N   VAL  361      11.923  60.466  30.569  1.00 28.39
ATOM   2766  CA  VAL  361      13.248  59.971  30.219  1.00 28.01
ATOM   2767  CB  VAL  361      14.258  60.256  31.342  1.00 27.73
ATOM   2768  CG1 VAL  361      15.575  59.551  31.055  1.00 27.43
```

Figure 4

```
ATOM   2769  CG2 VAL   361      14.492  61.759  31.453  1.00 27.76
ATOM   2770  C   VAL   361      13.245  58.464  29.919  1.00 27.74
ATOM   2771  O   VAL   361      14.055  57.982  29.107  1.00 27.40
ATOM   2772  N   ARG   362      12.341  57.719  30.556  1.00 27.72
ATOM   2773  CA  ARG   362      12.277  56.275  30.325  1.00 27.95
ATOM   2774  CB  ARG   362      11.523  55.571  31.455  1.00 29.48
ATOM   2775  CG  ARG   362      11.137  54.147  31.101  1.00 31.97
ATOM   2776  CD  ARG   362      10.900  53.266  32.308  1.00 33.93
ATOM   2777  NE  ARG   362      10.930  51.859  31.893  1.00 37.37
ATOM   2778  CZ  ARG   362      10.938  50.817  32.725  1.00 37.52
ATOM   2779  NH1 ARG   362      10.920  51.010  34.043  1.00 38.72
ATOM   2780  NH2 ARG   362      10.960  49.582  32.230  1.00 36.06
ATOM   2781  C   ARG   362      11.614  55.959  28.994  1.00 27.88
ATOM   2782  O   ARG   362      12.016  55.032  28.289  1.00 29.02
ATOM   2783  N   ARG   363      10.586  56.728  28.660  1.00 27.31
ATOM   2784  CA  ARG   363       9.866  56.564  27.400  1.00 25.77
ATOM   2785  CB  ARG   363       8.641  57.486  27.374  1.00 26.51
ATOM   2786  CG  ARG   363       7.530  57.084  28.318  1.00 26.30
ATOM   2787  CD  ARG   363       6.730  55.929  27.739  1.00 28.36
ATOM   2788  NE  ARG   363       6.259  56.216  26.380  1.00 30.91
ATOM   2789  CZ  ARG   363       6.872  55.826  25.260  1.00 31.55
ATOM   2790  NH1 ARG   363       7.992  55.112  25.315  1.00 33.18
ATOM   2791  NH2 ARG   363       6.370  56.158  24.077  1.00 32.30
ATOM   2792  C   ARG   363      10.817  56.949  26.272  1.00 24.71
ATOM   2793  O   ARG   363      10.748  56.392  25.175  1.00 24.40
ATOM   2794  N   ALA   364      11.706  57.905  26.540  1.00 23.90
ATOM   2795  CA  ALA   364      12.653  58.339  25.507  1.00 24.48
ATOM   2796  CB  ALA   364      13.463  59.545  25.969  1.00 23.15
ATOM   2797  C   ALA   364      13.571  57.176  25.226  1.00 25.01
ATOM   2798  O   ALA   364      13.854  56.872  24.069  1.00 26.22
ATOM   2799  N   CYS   365      14.023  56.518  26.290  1.00 25.03
ATOM   2800  CA  CYS   365      14.902  55.370  26.157  1.00 24.77
ATOM   2801  CB  CYS   365      15.450  54.970  27.528  1.00 23.03
ATOM   2802  SG  CYS   365      16.728  56.114  28.173  1.00 21.60
ATOM   2803  C   CYS   365      14.140  54.206  25.514  1.00 26.44
ATOM   2804  O   CYS   365      14.661  53.535  24.617  1.00 27.49
ATOM   2805  N   GLU   366      12.906  53.956  25.944  1.00 26.87
ATOM   2806  CA  GLU   366      12.145  52.859  25.342  1.00 27.98
ATOM   2807  CB  GLU   366      10.757  52.743  25.988  1.00 28.74
ATOM   2808  CG  GLU   366      10.785  52.431  27.490  1.00 30.75
ATOM   2809  CD  GLU   366       9.427  51.981  28.041  1.00 32.09
ATOM   2810  OE1 GLU   366       8.444  52.757  27.970  1.00 32.39
ATOM   2811  OE2 GLU   366       9.342  50.841  28.547  1.00 33.30
ATOM   2812  C   GLU   366      12.005  53.056  23.815  1.00 28.15
ATOM   2813  O   GLU   366      12.117  52.104  23.029  1.00 27.63
ATOM   2814  N   SER   367      11.776  54.304  23.407  1.00 28.42
ATOM   2815  CA  SER   367      11.612  54.650  21.993  1.00 27.23
ATOM   2816  CB  SER   367      11.368  56.156  21.833  1.00 27.45
ATOM   2817  OG  SER   367      10.161  56.552  22.447  1.00 27.44
ATOM   2818  C   SER   367      12.824  54.276  21.165  1.00 26.52
ATOM   2819  O   SER   367      12.724  53.567  20.162  1.00 27.99
ATOM   2820  N   VAL   368      13.977  54.773  21.581  1.00 24.30
ATOM   2821  CA  VAL   368      15.194  54.499  20.849  1.00 22.45
ATOM   2822  CB  VAL   368      16.324  55.395  21.375  1.00 20.96
ATOM   2823  CG1 VAL   368      17.623  55.075  20.682  1.00 18.44
ATOM   2824  CG2 VAL   368      15.928  56.843  21.190  1.00 18.99
ATOM   2825  C   VAL   368      15.605  53.019  20.888  1.00 23.13
ATOM   2826  O   VAL   368      15.850  52.420  19.832  1.00 23.88
ATOM   2827  N   SER   369      15.660  52.405  22.071  1.00 22.54
```

Figure 4


```
ATOM   2828  CA  SER  369      16.071  51.003  22.106  1.00 21.93
ATOM   2829  CB  SER  369      16.248  50.476  23.542  1.00 23.39
ATOM   2830  OG  SER  369      15.011  50.251  24.197  1.00 25.91
ATOM   2831  C   SER  369      15.109  50.112  21.348  1.00 20.54
ATOM   2832  O   SER  369      15.526  49.063  20.850  1.00 20.31
ATOM   2833  N   THR  370      13.832  50.499  21.259  1.00 18.40
ATOM   2834  CA  THR  370      12.878  49.682  20.496  1.00 17.32
ATOM   2835  CB  THR  370      11.400  49.976  20.859  1.00 16.46
ATOM   2836  OG1 THR  370      11.053  49.298  22.073  1.00 15.81
ATOM   2837  CG2 THR  370      10.473  49.487  19.774  1.00 14.39
ATOM   2838  C   THR  370      13.076  49.936  19.001  1.00 17.03
ATOM   2839  O   THR  370      12.977  49.008  18.186  1.00 17.38
ATOM   2840  N   ARG  371      13.358  51.177  18.617  1.00 16.71
ATOM   2841  CA  ARG  371      13.562  51.423  17.201  1.00 16.54
ATOM   2842  CB  ARG  371      13.810  52.905  16.882  1.00 17.42
ATOM   2843  CG  ARG  371      14.013  53.123  15.374  1.00 17.76
ATOM   2844  CD  ARG  371      14.283  54.559  14.943  1.00 17.40
ATOM   2845  NE  ARG  371      15.567  55.076  15.412  1.00 18.85
ATOM   2846  CZ  ARG  371      16.159  56.154  14.896  1.00 18.99
ATOM   2847  NH1 ARG  371      15.583  56.810  13.892  1.00 17.43
ATOM   2848  NH2 ARG  371      17.303  56.605  15.406  1.00 19.19
ATOM   2849  C   ARG  371      14.763  50.607  16.759  1.00 15.91
ATOM   2850  O   ARG  371      14.689  49.929  15.748  1.00 17.14
ATOM   2851  N   ALA  372      15.856  50.644  17.519  1.00 15.40
ATOM   2852  CA  ALA  372      17.061  49.883  17.148  1.00 16.23
ATOM   2853  CB  ALA  372      18.152  50.046  18.197  1.00 15.66
ATOM   2854  C   ALA  372      16.775  48.407  16.957  1.00 16.83
ATOM   2855  O   ALA  372      17.125  47.838  15.923  1.00 18.06
ATOM   2856  N   ALA  373      16.149  47.790  17.955  1.00 16.86
ATOM   2857  CA  ALA  373      15.817  46.367  17.912  1.00 17.10
ATOM   2858  CB  ALA  373      15.027  45.976  19.156  1.00 16.66
ATOM   2859  C   ALA  373      15.024  46.018  16.665  1.00 18.79
ATOM   2860  O   ALA  373      15.301  45.004  16.018  1.00 20.02
ATOM   2861  N   HIS  374      14.037  46.841  16.316  1.00 19.22
ATOM   2862  CA  HIS  374      13.243  46.560  15.122  1.00 20.89
ATOM   2863  CB  HIS  374      12.025  47.489  15.052  1.00 20.98
ATOM   2864  CG  HIS  374      10.948  47.131  16.029  1.00 19.79
ATOM   2865  CD2 HIS  374      10.813  46.065  16.855  1.00 19.53
ATOM   2866  ND1 HIS  374       9.833  47.914  16.229  1.00 19.92
ATOM   2867  CE1 HIS  374       9.057  47.347  17.137  1.00 18.78
ATOM   2868  NE2 HIS  374       9.629  46.223  17.532  1.00 18.61
ATOM   2869  C   HIS  374      14.075  46.696  13.866  1.00 21.57
ATOM   2870  O   HIS  374      14.136  45.789  13.058  1.00 21.42
ATOM   2871  N   MSE  375      14.722  47.835  13.698  1.00 24.00
ATOM   2872  CA  MSE  375      15.561  48.027  12.528  1.00 26.05
ATOM   2873  CB  MSE  375      16.390  49.311  12.666  1.00 28.31
ATOM   2874  CG  MSE  375      15.671  50.558  12.197  1.00 31.46
ATOM   2875  SE  MSE  375      15.246  50.448  10.400  1.00 41.26
ATOM   2876  CE  MSE  375      16.340  51.745   9.680  1.00 36.51
ATOM   2877  C   MSE  375      16.476  46.810  12.390  1.00 25.84
ATOM   2878  O   MSE  375      16.501  46.159  11.351  1.00 26.84
ATOM   2879  N   CYS  376      17.200  46.489  13.455  1.00 25.61
ATOM   2880  CA  CYS  376      18.107  45.349  13.436  1.00 25.11
ATOM   2881  CB  CYS  376      18.693  45.117  14.831  1.00 26.04
ATOM   2882  SG  CYS  376      20.038  43.879  14.876  1.00 27.98
ATOM   2883  C   CYS  376      17.445  44.058  12.931  1.00 24.01
ATOM   2884  O   CYS  376      18.015  43.369  12.078  1.00 24.35
ATOM   2885  N   SER  377      16.251  43.741  13.443  1.00 22.14
ATOM   2886  CA  SER  377      15.519  42.531  13.038  1.00 20.58
```

Figure 4

```
ATOM   2887  CB  SER   377      14.203  42.399  13.811  1.00 20.36
ATOM   2888  OG  SER   377      13.233  43.325  13.338  1.00 20.95
ATOM   2889  C   SER   377      15.210  42.535  11.542  1.00 20.00
ATOM   2890  O   SER   377      15.154  41.484  10.900  1.00 19.23
ATOM   2891  N   ALA   378      14.995  43.715  10.980  1.00 19.64
ATOM   2892  CA  ALA   378      14.723  43.787   9.549  1.00 19.32
ATOM   2893  CB  ALA   378      14.521  45.243   9.119  1.00 18.02
ATOM   2894  C   ALA   378      15.958  43.186   8.874  1.00 19.40
ATOM   2895  O   ALA   378      15.860  42.230   8.093  1.00 18.55
ATOM   2896  N   GLY   379      17.123  43.740   9.222  1.00 20.18
ATOM   2897  CA  GLY   379      18.381  43.271   8.669  1.00 20.06
ATOM   2898  C   GLY   379      18.547  41.762   8.734  1.00 19.52
ATOM   2899  O   GLY   379      18.754  41.113   7.704  1.00 20.07
ATOM   2900  N   LEU   380      18.442  41.201   9.936  1.00 18.61
ATOM   2901  CA  LEU   380      18.596  39.763  10.110  1.00 18.74
ATOM   2902  CB  LEU   380      18.489  39.371  11.579  1.00 18.49
ATOM   2903  CG  LEU   380      18.774  37.881  11.816  1.00 17.82
ATOM   2904  CD1 LEU   380      20.215  37.586  11.383  1.00 16.94
ATOM   2905  CD2 LEU   380      18.557  37.512  13.285  1.00 16.34
ATOM   2906  C   LEU   380      17.580  38.938   9.341  1.00 19.56
ATOM   2907  O   LEU   380      17.895  37.833   8.892  1.00 20.67
ATOM   2908  N   ALA   381      16.354  39.447   9.211  1.00 19.83
ATOM   2909  CA  ALA   381      15.311  38.713   8.496  1.00 20.17
ATOM   2910  CB  ALA   381      13.961  39.327   8.759  1.00 19.87
ATOM   2911  C   ALA   381      15.638  38.746   7.009  1.00 21.06
ATOM   2912  O   ALA   381      15.421  37.773   6.269  1.00 21.05
ATOM   2913  N   GLY   382      16.174  39.874   6.567  1.00 21.33
ATOM   2914  CA  GLY   382      16.561  39.965   5.175  1.00 22.63
ATOM   2915  C   GLY   382      17.670  38.954   4.903  1.00 23.10
ATOM   2916  O   GLY   382      17.708  38.319   3.832  1.00 23.74
ATOM   2917  N   VAL   383      18.579  38.778   5.859  1.00 21.83
ATOM   2918  CA  VAL   383      19.642  37.828   5.615  1.00 22.47
ATOM   2919  CB  VAL   383      20.786  37.967   6.643  1.00 22.80
ATOM   2920  CG1 VAL   383      21.737  36.777   6.525  1.00 21.04
ATOM   2921  CG2 VAL   383      21.562  39.298   6.396  1.00 21.85
ATOM   2922  C   VAL   383      19.075  36.423   5.639  1.00 22.92
ATOM   2923  O   VAL   383      19.199  35.681   4.675  1.00 23.65
ATOM   2924  N   ILE   384      18.414  36.061   6.724  1.00 23.52
ATOM   2925  CA  ILE   384      17.853  34.721   6.835  1.00 24.64
ATOM   2926  CB  ILE   384      17.124  34.551   8.179  1.00 24.17
ATOM   2927  CG2 ILE   384      16.533  33.143   8.283  1.00 22.50
ATOM   2928  CG1 ILE   384      18.112  34.810   9.318  1.00 23.69
ATOM   2929  CD1 ILE   384      17.476  34.861  10.661  1.00 24.39
ATOM   2930  C   ILE   384      16.910  34.324   5.691  1.00 26.04
ATOM   2931  O   ILE   384      17.029  33.233   5.144  1.00 26.98
ATOM   2932  N   ASN   385      15.974  35.182   5.310  1.00 26.88
ATOM   2933  CA  ASN   385      15.097  34.785   4.218  1.00 27.99
ATOM   2934  CB  ASN   385      13.984  35.819   3.998  1.00 25.92
ATOM   2935  CG  ASN   385      13.038  35.918   5.174  1.00 23.68
ATOM   2936  OD1 ASN   385      12.721  34.921   5.820  1.00 21.60
ATOM   2937  ND2 ASN   385      12.567  37.128   5.448  1.00 23.03
ATOM   2938  C   ASN   385      15.888  34.579   2.915  1.00 29.62
ATOM   2939  O   ASN   385      15.610  33.647   2.143  1.00 29.62
ATOM   2940  N   ARG   386      16.869  35.440   2.660  1.00 31.30
ATOM   2941  CA  ARG   386      17.660  35.301   1.442  1.00 33.07
ATOM   2942  CB  ARG   386      18.840  36.261   1.446  1.00 32.62
ATOM   2943  CG  ARG   386      19.697  36.147   0.214  1.00 33.28
ATOM   2944  CD  ARG   386      20.908  37.059   0.284  1.00 34.52
ATOM   2945  NE  ARG   386      21.923  36.698  -0.704  1.00 35.29
```

Figure 4


```
ATOM   2946  CZ  ARG   386      21.812  36.910  -2.014  1.00 36.32
ATOM   2947  NH1 ARG   386      20.729  37.492  -2.518  1.00 35.95
ATOM   2948  NH2 ARG   386      22.782  36.525  -2.832  1.00 37.07
ATOM   2949  C   ARG   386      18.178  33.875   1.362  1.00 34.69
ATOM   2950  O   ARG   386      18.077  33.232   0.320  1.00 35.70
ATOM   2951  N   MSE   387      18.710  33.383   2.480  1.00 35.94
ATOM   2952  CA  MSE   387      19.250  32.036   2.560  1.00 37.39
ATOM   2953  CB  MSE   387      19.903  31.828   3.927  1.00 39.78
ATOM   2954  CG  MSE   387      21.099  32.754   4.186  1.00 42.37
ATOM   2955  SE  MSE   387      21.873  32.552   5.859  1.00 49.18
ATOM   2956  CE  MSE   387      21.738  30.694   6.097  1.00 44.67
ATOM   2957  C   MSE   387      18.179  30.976   2.311  1.00 38.50
ATOM   2958  O   MSE   387      18.463  29.927   1.721  1.00 37.80
ATOM   2959  N   ARG   388      16.954  31.255   2.769  1.00 40.15
ATOM   2960  CA  ARG   388      15.808  30.352   2.586  1.00 41.28
ATOM   2961  CB  ARG   388      14.554  30.941   3.245  1.00 42.50
ATOM   2962  CG  ARG   388      13.268  30.115   3.069  1.00 42.73
ATOM   2963  CD  ARG   388      12.266  30.443   4.178  1.00 43.15
ATOM   2964  NE  ARG   388      10.965  29.787   4.012  1.00 44.47
ATOM   2965  CZ  ARG   388      10.049  30.134   3.104  1.00 44.46
ATOM   2966  NH1 ARG   388      10.283  31.139   2.269  1.00 44.11
ATOM   2967  NH2 ARG   388       8.895  29.478   3.033  1.00 44.15
ATOM   2968  C   ARG   388      15.579  30.210   1.094  1.00 41.39
ATOM   2969  O   ARG   388      15.516  29.104   0.554  1.00 40.76
ATOM   2970  N   GLU   389      15.460  31.355   0.439  1.00 41.88
ATOM   2971  CA  GLU   389      15.275  31.405  -0.997  1.00 43.37
ATOM   2972  CB  GLU   389      15.211  32.867  -1.448  1.00 45.21
ATOM   2973  CG  GLU   389      15.227  33.079  -2.957  1.00 48.22
ATOM   2974  CD  GLU   389      13.894  32.754  -3.632  1.00 50.35
ATOM   2975  OE1 GLU   389      13.850  32.799  -4.891  1.00 51.00
ATOM   2976  OE2 GLU   389      12.900  32.464  -2.912  1.00 50.86
ATOM   2977  C   GLU   389      16.476  30.713  -1.635  1.00 43.77
ATOM   2978  O   GLU   389      16.325  29.726  -2.355  1.00 43.53
ATOM   2979  N   SER   390      17.671  31.227  -1.335  1.00 43.84
ATOM   2980  CA  SER   390      18.925  30.697  -1.878  1.00 43.61
ATOM   2981  CB  SER   390      20.112  31.549  -1.425  1.00 43.41
ATOM   2982  OG  SER   390      20.229  32.703  -2.241  1.00 43.45
ATOM   2983  C   SER   390      19.243  29.234  -1.607  1.00 43.62
ATOM   2984  O   SER   390      20.126  28.671  -2.251  1.00 44.11
ATOM   2985  N   ARG   391      18.555  28.614  -0.660  1.00 43.22
ATOM   2986  CA  ARG   391      18.815  27.213  -0.396  1.00 43.67
ATOM   2987  CB  ARG   391      19.174  26.994   1.078  1.00 42.72
ATOM   2988  CG  ARG   391      20.440  27.699   1.512  1.00 41.51
ATOM   2989  CD  ARG   391      20.907  27.245   2.892  1.00 39.51
ATOM   2990  NE  ARG   391      22.183  27.864   3.231  1.00 37.99
ATOM   2991  CZ  ARG   391      22.940  27.512   4.266  1.00 37.81
ATOM   2992  NH1 ARG   391      22.545  26.540   5.070  1.00 36.05
ATOM   2993  NH2 ARG   391      24.105  28.121   4.482  1.00 37.12
ATOM   2994  C   ARG   391      17.578  26.404  -0.756  1.00 44.95
ATOM   2995  O   ARG   391      17.458  25.241  -0.372  1.00 45.05
ATOM   2996  N   SER   392      16.666  27.023  -1.502  1.00 46.71
ATOM   2997  CA  SER   392      15.420  26.367  -1.895  1.00 48.25
ATOM   2998  CB  SER   392      15.631  25.468  -3.121  1.00 48.10
ATOM   2999  OG  SER   392      15.610  26.216  -4.326  1.00 48.60
ATOM   3000  C   SER   392      14.880  25.536  -0.737  1.00 49.61
ATOM   3001  O   SER   392      14.601  24.344  -0.882  1.00 49.37
ATOM   3002  N   GLU   393      14.749  26.175   0.420  1.00 51.58
ATOM   3003  CA  GLU   393      14.237  25.510   1.617  1.00 53.54
ATOM   3004  CB  GLU   393      15.085  25.897   2.842  1.00 54.33
```

Figure 4


```
ATOM   3005  CG  GLU 393      16.586  25.655   2.701  1.00 54.92
ATOM   3006  CD  GLU 393      17.057  24.420   3.450  1.00 55.87
ATOM   3007  OE1 GLU 393      16.845  24.347   4.683  1.00 55.29
ATOM   3008  OE2 GLU 393      17.646  23.523   2.806  1.00 56.69
ATOM   3009  C   GLU 393      12.793  25.961   1.838  1.00 54.20
ATOM   3010  O   GLU 393      12.482  27.151   1.693  1.00 53.70
ATOM   3011  N   ASP 394      11.907  25.026   2.173  1.00 55.42
ATOM   3012  CA  ASP 394      10.519  25.404   2.419  1.00 56.88
ATOM   3013  CB  ASP 394       9.585  24.194   2.400  1.00 58.69
ATOM   3014  CG  ASP 394       8.111  24.602   2.415  1.00 61.23
ATOM   3015  OD1 ASP 394       7.691  25.298   3.376  1.00 62.29
ATOM   3016  OD2 ASP 394       7.374  24.237   1.466  1.00 62.03
ATOM   3017  C   ASP 394      10.489  26.041   3.795  1.00 56.57
ATOM   3018  O   ASP 394      10.023  27.164   3.959  1.00 56.22
ATOM   3019  N   VAL 395      10.994  25.298   4.773  1.00 56.79
ATOM   3020  CA  VAL 395      11.086  25.756   6.153  1.00 57.23
ATOM   3021  CB  VAL 395      10.166  24.949   7.093  1.00 57.72
ATOM   3022  CG1 VAL 395      10.444  25.320   8.548  1.00 57.64
ATOM   3023  CG2 VAL 395       8.708  25.221   6.749  1.00 58.46
ATOM   3024  C   VAL 395      12.534  25.538   6.575  1.00 57.01
ATOM   3025  O   VAL 395      12.968  24.407   6.793  1.00 56.90
ATOM   3026  N   MSE 396      13.280  26.626   6.690  1.00 56.80
ATOM   3027  CA  MSE 396      14.682  26.536   7.058  1.00 56.12
ATOM   3028  CB  MSE 396      15.463  27.645   6.375  1.00 57.66
ATOM   3029  CG  MSE 396      16.932  27.623   6.690  1.00 60.51
ATOM   3030  SE  MSE 396      17.716  29.077   6.002  1.00 65.26
ATOM   3031  CE  MSE 396      17.988  28.564   4.293  1.00 64.74
ATOM   3032  C   MSE 396      14.964  26.600   8.545  1.00 54.59
ATOM   3033  O   MSE 396      14.487  27.491   9.245  1.00 54.08
ATOM   3034  N   ARG 397      15.740  25.637   9.025  1.00 53.05
ATOM   3035  CA  ARG 397      16.134  25.613  10.426  1.00 51.13
ATOM   3036  CB  ARG 397      16.226  24.181  10.951  1.00 52.77
ATOM   3037  CG  ARG 397      14.888  23.520  11.244  1.00 55.36
ATOM   3038  CD  ARG 397      15.132  22.079  11.671  1.00 58.69
ATOM   3039  NE  ARG 397      13.985  21.448  12.326  1.00 61.28
ATOM   3040  CZ  ARG 397      14.056  20.294  12.990  1.00 62.10
ATOM   3041  NH1 ARG 397      15.215  19.651  13.078  1.00 62.57
ATOM   3042  NH2 ARG 397      12.978  19.793  13.583  1.00 62.49
ATOM   3043  C   ARG 397      17.509  26.252  10.397  1.00 48.33
ATOM   3044  O   ARG 397      18.273  26.029   9.466  1.00 47.77
ATOM   3045  N   ILE 398      17.825  27.064  11.395  1.00 45.82
ATOM   3046  CA  ILE 398      19.120  27.721  11.396  1.00 43.01
ATOM   3047  CB  ILE 398      19.202  28.791  10.293  1.00 43.25
ATOM   3048  CG2 ILE 398      18.161  29.864  10.532  1.00 43.18
ATOM   3049  CG1 ILE 398      20.594  29.417  10.279  1.00 43.75
ATOM   3050  CD1 ILE 398      20.768  30.466   9.206  1.00 44.64
ATOM   3051  C   ILE 398      19.441  28.381  12.717  1.00 40.64
ATOM   3052  O   ILE 398      18.557  28.890  13.404  1.00 40.10
ATOM   3053  N   THR 399      20.722  28.360  13.060  1.00 37.78
ATOM   3054  CA  THR 399      21.185  28.954  14.290  1.00 35.36
ATOM   3055  CB  THR 399      22.052  27.988  15.079  1.00 35.02
ATOM   3056  OG1 THR 399      21.280  26.832  15.425  1.00 34.92
ATOM   3057  CG2 THR 399      22.570  28.666  16.345  1.00 34.73
ATOM   3058  C   THR 399      22.001  30.197  13.994  1.00 34.71
ATOM   3059  O   THR 399      22.736  30.254  13.005  1.00 35.10
ATOM   3060  N   VAL 400      21.858  31.184  14.871  1.00 32.96
ATOM   3061  CA  VAL 400      22.539  32.457  14.759  1.00 31.07
ATOM   3062  CB  VAL 400      21.514  33.593  14.592  1.00 31.21
ATOM   3063  CG1 VAL 400      22.211  34.934  14.415  1.00 31.76
```

Figure 4


```
ATOM   3064  CG2 VAL   400      20.628  33.298  13.405  1.00 31.47
ATOM   3065  C   VAL   400      23.336  32.685  16.039  1.00 30.19
ATOM   3066  O   VAL   400      22.779  32.640  17.144  1.00 30.96
ATOM   3067  N   GLY   401      24.641  32.905  15.888  1.00 28.35
ATOM   3068  CA  GLY   401      25.482  33.150  17.041  1.00 24.47
ATOM   3069  C   GLY   401      25.487  34.641  17.235  1.00 23.04
ATOM   3070  O   GLY   401      25.595  35.388  16.260  1.00 20.38
ATOM   3071  N   VAL   402      25.367  35.086  18.482  1.00 23.36
ATOM   3072  CA  VAL   402      25.338  36.514  18.751  1.00 23.38
ATOM   3073  CB  VAL   402      23.927  36.960  19.124  1.00 22.79
ATOM   3074  CG1 VAL   402      23.790  38.458  18.909  1.00 22.85
ATOM   3075  CG2 VAL   402      22.895  36.176  18.320  1.00 22.42
ATOM   3076  C   VAL   402      26.252  36.899  19.893  1.00 24.25
ATOM   3077  O   VAL   402      26.484  36.098  20.794  1.00 25.20
ATOM   3078  N   ASP   403      26.770  38.124  19.848  1.00 24.83
ATOM   3079  CA  ASP   403      27.637  38.649  20.894  1.00 27.11
ATOM   3080  CB  ASP   403      29.078  38.212  20.691  1.00 30.98
ATOM   3081  CG  ASP   403      30.003  38.739  21.787  1.00 34.48
ATOM   3082  OD1 ASP   403      29.887  39.938  22.122  1.00 36.02
ATOM   3083  OD2 ASP   403      30.842  37.960  22.311  1.00 36.05
ATOM   3084  C   ASP   403      27.562  40.154  20.763  1.00 27.24
ATOM   3085  O   ASP   403      27.550  40.667  19.645  1.00 29.15
ATOM   3086  N   GLY   404      27.519  40.863  21.888  1.00 26.60
ATOM   3087  CA  GLY   404      27.410  42.316  21.863  1.00 26.50
ATOM   3088  C   GLY   404      26.750  42.829  23.137  1.00 27.10
ATOM   3089  O   GLY   404      25.810  42.193  23.665  1.00 26.90
ATOM   3090  N   SER   405      27.209  43.972  23.644  1.00 26.72
ATOM   3091  CA  SER   405      26.638  44.496  24.887  1.00 27.96
ATOM   3092  CB  SER   405      27.409  45.722  25.371  1.00 28.04
ATOM   3093  OG  SER   405      27.164  46.828  24.521  1.00 30.53
ATOM   3094  C   SER   405      25.168  44.857  24.738  1.00 28.25
ATOM   3095  O   SER   405      24.341  44.473  25.573  1.00 27.96
ATOM   3096  N   VAL   406      24.844  45.591  23.675  1.00 27.79
ATOM   3097  CA  VAL   406      23.465  45.992  23.445  1.00 28.13
ATOM   3098  CB  VAL   406      23.281  46.667  22.074  1.00 28.02
ATOM   3099  CG1 VAL   406      21.814  47.063  21.908  1.00 27.91
ATOM   3100  CG2 VAL   406      24.197  47.877  21.940  1.00 26.07
ATOM   3101  C   VAL   406      22.535  44.789  23.488  1.00 28.35
ATOM   3102  O   VAL   406      21.484  44.826  24.120  1.00 28.48
ATOM   3103  N   TYR   407      22.934  43.718  22.811  1.00 28.72
ATOM   3104  CA  TYR   407      22.130  42.493  22.736  1.00 28.45
ATOM   3105  CB  TYR   407      22.613  41.643  21.558  1.00 26.86
ATOM   3106  CG  TYR   407      21.831  40.373  21.341  1.00 25.29
ATOM   3107  CD1 TYR   407      20.700  40.358  20.535  1.00 25.44
ATOM   3108  CE1 TYR   407      19.964  39.189  20.346  1.00 25.93
ATOM   3109  CD2 TYR   407      22.213  39.192  21.955  1.00 24.93
ATOM   3110  CE2 TYR   407      21.488  38.021  21.780  1.00 25.18
ATOM   3111  CZ  TYR   407      20.362  38.024  20.974  1.00 26.03
ATOM   3112  OH  TYR   407      19.626  36.868  20.822  1.00 25.67
ATOM   3113  C   TYR   407      22.175  41.651  24.014  1.00 28.83
ATOM   3114  O   TYR   407      21.202  40.988  24.369  1.00 28.62
ATOM   3115  N   LYS   408      23.306  41.674  24.705  1.00 29.64
ATOM   3116  CA  LYS   408      23.440  40.881  25.916  1.00 30.07
ATOM   3117  CB  LYS   408      24.904  40.477  26.118  1.00 30.08
ATOM   3118  CG  LYS   408      25.442  39.556  25.030  1.00 30.61
ATOM   3119  CD  LYS   408      26.597  38.698  25.529  1.00 30.05
ATOM   3120  CE  LYS   408      26.799  37.515  24.601  1.00 30.22
ATOM   3121  NZ  LYS   408      27.828  36.573  25.097  1.00 30.20
ATOM   3122  C   LYS   408      22.940  41.551  27.185  1.00 30.82
```

Figure 4


```
ATOM   3123  O   LYS  408      22.327  40.901  28.038  1.00 31.98
ATOM   3124  N   LEU  409      23.176  42.853  27.296  1.00 30.97
ATOM   3125  CA  LEU  409      22.823  43.598  28.501  1.00 31.11
ATOM   3126  CB  LEU  409      24.006  44.482  28.875  1.00 30.54
ATOM   3127  CG  LEU  409      25.305  43.700  28.962  1.00 29.31
ATOM   3128  CD1 LEU  409      26.372  44.591  29.597  1.00 29.41
ATOM   3129  CD2 LEU  409      25.067  42.423  29.785  1.00 28.16
ATOM   3130  C   LEU  409      21.548  44.441  28.611  1.00 31.44
ATOM   3131  O   LEU  409      20.978  44.542  29.708  1.00 31.86
ATOM   3132  N   HIS  410      21.122  45.077  27.519  1.00 31.34
ATOM   3133  CA  HIS  410      19.929  45.912  27.572  1.00 30.80
ATOM   3134  CB  HIS  410      19.732  46.635  26.247  1.00 30.36
ATOM   3135  CG  HIS  410      18.703  47.717  26.303  1.00 29.89
ATOM   3136  CD2 HIS  410      18.815  49.060  26.179  1.00 29.29
ATOM   3137  ND1 HIS  410      17.362  47.457  26.508  1.00 30.79
ATOM   3138  CE1 HIS  410      16.691  48.595  26.505  1.00 29.88
ATOM   3139  NE2 HIS  410      17.548  49.583  26.309  1.00 30.87
ATOM   3140  C   HIS  410      18.728  45.031  27.900  1.00 31.41
ATOM   3141  O   HIS  410      18.467  44.055  27.207  1.00 31.97
ATOM   3142  N   PRO  411      17.985  45.376  28.969  1.00 31.63
ATOM   3143  CD  PRO  411      18.173  46.690  29.610  1.00 31.32
ATOM   3144  CA  PRO  411      16.798  44.708  29.518  1.00 31.33
ATOM   3145  CB  PRO  411      16.111  45.815  30.299  1.00 31.27
ATOM   3146  CG  PRO  411      17.257  46.599  30.822  1.00 32.32
ATOM   3147  C   PRO  411      15.827  44.037  28.571  1.00 32.09
ATOM   3148  O   PRO  411      15.362  42.920  28.838  1.00 32.76
ATOM   3149  N   SER  412      15.519  44.684  27.457  1.00 31.73
ATOM   3150  CA  SER  412      14.527  44.094  26.573  1.00 31.92
ATOM   3151  CB  SER  412      13.210  44.834  26.771  1.00 32.51
ATOM   3152  OG  SER  412      13.368  46.200  26.390  1.00 33.27
ATOM   3153  C   SER  412      14.838  44.047  25.082  1.00 31.91
ATOM   3154  O   SER  412      14.039  43.520  24.304  1.00 32.59
ATOM   3155  N   PHE  413      15.974  44.601  24.679  1.00 30.72
ATOM   3156  CA  PHE  413      16.348  44.615  23.271  1.00 30.13
ATOM   3157  CB  PHE  413      17.778  45.105  23.130  1.00 28.18
ATOM   3158  CG  PHE  413      18.213  45.285  21.716  1.00 25.96
ATOM   3159  CD1 PHE  413      18.085  46.522  21.094  1.00 25.70
ATOM   3160  CD2 PHE  413      18.772  44.233  21.015  1.00 24.47
ATOM   3161  CE1 PHE  413      18.517  46.711  19.787  1.00 25.13
ATOM   3162  CE2 PHE  413      19.208  44.408  19.707  1.00 24.84
ATOM   3163  CZ  PHE  413      19.082  45.652  19.092  1.00 24.48
ATOM   3164  C   PHE  413      16.232  43.228  22.645  1.00 31.20
ATOM   3165  O   PHE  413      15.571  43.026  21.612  1.00 31.56
ATOM   3166  N   LYS  414      16.888  42.268  23.275  1.00 31.75
ATOM   3167  CA  LYS  414      16.851  40.906  22.790  1.00 32.75
ATOM   3168  CB  LYS  414      17.626  39.999  23.755  1.00 33.66
ATOM   3169  CG  LYS  414      17.570  38.526  23.429  1.00 34.45
ATOM   3170  CD  LYS  414      18.732  37.744  24.049  1.00 36.05
ATOM   3171  CE  LYS  414      18.845  37.909  25.558  1.00 35.80
ATOM   3172  NZ  LYS  414      19.972  38.817  25.920  1.00 36.66
ATOM   3173  C   LYS  414      15.412  40.411  22.600  1.00 33.19
ATOM   3174  O   LYS  414      15.054  39.927  21.518  1.00 33.30
ATOM   3175  N   GLU  415      14.577  40.542  23.627  1.00 33.81
ATOM   3176  CA  GLU  415      13.193  40.071  23.513  1.00 34.53
ATOM   3177  CB  GLU  415      12.462  40.251  24.838  1.00 37.66
ATOM   3178  CG  GLU  415      13.062  39.497  26.002  1.00 42.83
ATOM   3179  CD  GLU  415      14.376  40.090  26.520  1.00 45.68
ATOM   3180  OE1 GLU  415      14.523  41.339  26.526  1.00 47.31
ATOM   3181  OE2 GLU  415      15.245  39.293  26.956  1.00 47.44
```

Figure 4

ATOM	3182	C	GLU	415	12.409	40.776	22.401	1.00	33.23
ATOM	3183	O	GLU	415	11.676	40.137	21.649	1.00	33.06
ATOM	3184	N	ARG	416	12.551	42.092	22.299	1.00	31.77
ATOM	3185	CA	ARG	416	11.841	42.825	21.264	1.00	30.32
ATOM	3186	CB	ARG	416	12.066	44.328	21.427	1.00	31.27
ATOM	3187	CG	ARG	416	11.645	44.875	22.796	1.00	33.92
ATOM	3188	CD	ARG	416	11.783	46.393	22.901	1.00	35.48
ATOM	3189	NE	ARG	416	11.545	46.866	24.267	1.00	38.24
ATOM	3190	CZ	ARG	416	11.982	48.030	24.746	1.00	39.11
ATOM	3191	NH1	ARG	416	12.676	48.850	23.967	1.00	39.89
ATOM	3192	NH2	ARG	416	11.754	48.365	26.009	1.00	38.52
ATOM	3193	C	ARG	416	12.379	42.354	19.916	1.00	29.08
ATOM	3194	O	ARG	416	11.620	42.159	18.964	1.00	28.85
ATOM	3195	N	PHE	417	13.694	42.144	19.862	1.00	27.59
ATOM	3196	CA	PHE	417	14.377	41.707	18.648	1.00	25.70
ATOM	3197	CB	PHE	417	15.886	41.687	18.890	1.00	23.64
ATOM	3198	CG	PHE	417	16.687	41.310	17.680	1.00	20.59
ATOM	3199	CD1	PHE	417	16.910	42.230	16.671	1.00	18.99
ATOM	3200	CD2	PHE	417	17.183	40.018	17.540	1.00	19.41
ATOM	3201	CE1	PHE	417	17.610	41.870	15.540	1.00	19.87
ATOM	3202	CE2	PHE	417	17.884	39.641	16.413	1.00	18.04
ATOM	3203	CZ	PHE	417	18.100	40.563	15.409	1.00	20.04
ATOM	3204	C	PHE	417	13.943	40.342	18.099	1.00	25.74
ATOM	3205	O	PHE	417	13.568	40.225	16.927	1.00	25.24
ATOM	3206	N	HIS	418	14.012	39.301	18.922	1.00	26.11
ATOM	3207	CA	HIS	418	13.612	37.962	18.459	1.00	26.79
ATOM	3208	CB	HIS	418	13.638	36.973	19.615	1.00	28.01
ATOM	3209	CG	HIS	418	14.973	36.854	20.279	1.00	28.81
ATOM	3210	CD2	HIS	418	16.168	37.425	19.989	1.00	29.42
ATOM	3211	ND1	HIS	418	15.182	36.067	21.389	1.00	28.15
ATOM	3212	CE1	HIS	418	16.446	36.157	21.755	1.00	29.43
ATOM	3213	NE2	HIS	418	17.067	36.974	20.924	1.00	29.74
ATOM	3214	C	HIS	418	12.209	37.985	17.876	1.00	26.41
ATOM	3215	O	HIS	418	11.976	37.565	16.733	1.00	26.40
ATOM	3216	N	ALA	419	11.284	38.487	18.688	1.00	25.83
ATOM	3217	CA	ALA	419	9.885	38.603	18.328	1.00	25.05
ATOM	3218	CB	ALA	419	9.182	39.454	19.352	1.00	24.80
ATOM	3219	C	ALA	419	9.731	39.215	16.943	1.00	25.35
ATOM	3220	O	ALA	419	9.146	38.601	16.029	1.00	25.99
ATOM	3221	N	SER	420	10.249	40.425	16.777	1.00	25.26
ATOM	3222	CA	SER	420	10.159	41.078	15.481	1.00	25.31
ATOM	3223	CB	SER	420	10.897	42.405	15.515	1.00	23.85
ATOM	3224	OG	SER	420	10.692	43.089	14.303	1.00	23.43
ATOM	3225	C	SER	420	10.751	40.170	14.391	1.00	26.14
ATOM	3226	O	SER	420	10.145	39.976	13.331	1.00	25.95
ATOM	3227	N	VAL	421	11.926	39.602	14.670	1.00	27.34
ATOM	3228	CA	VAL	421	12.602	38.699	13.733	1.00	28.41
ATOM	3229	CB	VAL	421	13.919	38.127	14.346	1.00	27.63
ATOM	3230	CG1	VAL	421	14.479	37.020	13.475	1.00	26.36
ATOM	3231	CG2	VAL	421	14.953	39.232	14.469	1.00	28.22
ATOM	3232	C	VAL	421	11.689	37.535	13.325	1.00	29.65
ATOM	3233	O	VAL	421	11.557	37.227	12.130	1.00	28.72
ATOM	3234	N	ARG	422	11.069	36.886	14.310	1.00	30.74
ATOM	3235	CA	ARG	422	10.165	35.775	14.014	1.00	32.79
ATOM	3236	CB	ARG	422	9.419	35.328	15.265	1.00	33.29
ATOM	3237	CG	ARG	422	10.259	35.197	16.512	1.00	34.47
ATOM	3238	CD	ARG	422	11.081	33.927	16.558	1.00	34.54
ATOM	3239	NE	ARG	422	11.862	33.905	17.795	1.00	35.75
ATOM	3240	CZ	ARG	422	12.824	33.028	18.066	1.00	35.45

Figure 4

	ATOM	3241	NH1	ARG	422	13.127	32.085	17.180	1.00	35.35
	ATOM	3242	NH2	ARG	422	13.490	33.108	19.215	1.00	33.55
	ATOM	3243	C	ARG	422	9.123	36.277	13.019	1.00	33.41
	ATOM	3244	O	ARG	422	8.949	35.728	11.929	1.00	33.68
5	ATOM	3245	N	ARG	423	8.446	37.348	13.417	1.00	34.00
	ATOM	3246	CA	ARG	423	7.394	37.946	12.622	1.00	34.13
	ATOM	3247	CB	ARG	423	7.022	39.301	13.207	1.00	35.16
	ATOM	3248	CG	ARG	423	5.538	39.584	13.202	1.00	36.10
	ATOM	3249	CD	ARG	423	5.212	40.831	14.012	1.00	37.57
10	ATOM	3250	NE	ARG	423	5.482	40.682	15.441	1.00	38.90
	ATOM	3251	CZ	ARG	423	6.274	41.503	16.133	1.00	40.51
	ATOM	3252	NH1	ARG	423	6.874	42.523	15.513	1.00	41.42
	ATOM	3253	NH2	ARG	423	6.461	41.324	17.440	1.00	38.76
	ATOM	3254	C	ARG	423	7.754	38.100	11.165	1.00	33.94
15	ATOM	3255	O	ARG	423	6.919	37.849	10.295	1.00	35.59
	ATOM	3256	N	LEU	424	8.993	38.494	10.884	1.00	32.85
	ATOM	3257	CA	LEU	424	9.418	38.699	9.497	1.00	31.57
	ATOM	3258	CB	LEU	424	10.474	39.788	9.450	1.00	28.75
	ATOM	3259	CG	LEU	424	10.030	41.129	10.003	1.00	27.64
20	ATOM	3260	CD1	LEU	424	11.220	42.080	10.066	1.00	26.47
	ATOM	3261	CD2	LEU	424	8.942	41.686	9.115	1.00	27.23
	ATOM	3262	C	LEU	424	9.950	37.479	8.747	1.00	32.00
	ATOM	3263	O	LEU	424	10.232	37.562	7.551	1.00	31.15
	ATOM	3264	N	THR	425	10.065	36.343	9.424	1.00	33.88
25	ATOM	3265	CA	THR	425	10.615	35.153	8.778	1.00	35.30
	ATOM	3266	CB	THR	425	11.886	34.722	9.495	1.00	35.17
	ATOM	3267	OG1	THR	425	11.580	34.463	10.874	1.00	35.24
	ATOM	3268	CG2	THR	425	12.939	35.817	9.399	1.00	35.16
	ATOM	3269	C	THR	425	9.711	33.923	8.675	1.00	37.00
30	ATOM	3270	O	THR	425	10.059	32.854	9.182	1.00	37.54
	ATOM	3271	N	PRO	426	8.562	34.040	7.982	1.00	38.04
	ATOM	3272	CD	PRO	426	8.144	35.123	7.073	1.00	38.49
	ATOM	3273	CA	PRO	426	7.663	32.890	7.856	1.00	38.85
	ATOM	3274	CB	PRO	426	6.745	33.295	6.700	1.00	38.23
35	ATOM	3275	CG	PRO	426	6.699	34.772	6.802	1.00	38.07
	ATOM	3276	C	PRO	426	8.445	31.615	7.527	1.00	39.83
	ATOM	3277	O	PRO	426	9.378	31.641	6.728	1.00	40.28
	ATOM	3278	N	SER	427	8.073	30.510	8.158	1.00	40.72
	ATOM	3279	CA	SER	427	8.713	29.232	7.892	1.00	41.82
40	ATOM	3280	CB	SER	427	8.358	28.785	6.474	1.00	42.86
	ATOM	3281	OG	SER	427	6.954	28.802	6.287	1.00	44.69
	ATOM	3282	C	SER	427	10.234	29.228	8.068	1.00	42.10
	ATOM	3283	O	SER	427	10.981	28.899	7.140	1.00	41.85
	ATOM	3284	N	CYS	428	10.679	29.586	9.267	1.00	42.60
45	ATOM	3285	CA	CYS	428	12.096	29.608	9.601	1.00	42.43
	ATOM	3286	CB	CYS	428	12.724	30.960	9.258	1.00	42.59
	ATOM	3287	SG	CYS	428	12.860	31.327	7.492	1.00	44.02
	ATOM	3288	C	CYS	428	12.195	29.381	11.096	1.00	42.45
	ATOM	3289	O	CYS	428	11.671	30.169	11.879	1.00	43.76
50	ATOM	3290	N	GLU	429	12.846	28.296	11.494	1.00	42.34
	ATOM	3291	CA	GLU	429	13.014	27.995	12.909	1.00	41.23
	ATOM	3292	CB	GLU	429	13.030	26.486	13.146	1.00	42.97
	ATOM	3293	CG	GLU	429	11.699	25.796	12.933	1.00	45.48
	ATOM	3294	CD	GLU	429	11.847	24.282	12.925	1.00	47.43
55	ATOM	3295	OE1	GLU	429	12.518	23.756	13.847	1.00	48.77
	ATOM	3296	OE2	GLU	429	11.298	23.623	12.005	1.00	48.07
	ATOM	3297	C	GLU	429	14.341	28.587	13.346	1.00	39.77
	ATOM	3298	O	GLU	429	15.370	27.902	13.352	1.00	39.92
	ATOM	3299	N	ILE	430	14.315	29.864	13.708	1.00	38.09

Figure 4

ATOM	3300	CA	ILE	430	15.514	30.560	14.142	1.00	36.48
ATOM	3301	CB	ILE	430	15.341	32.070	13.998	1.00	35.17
ATOM	3302	CG2	ILE	430	16.659	32.770	14.280	1.00	34.48
ATOM	3303	CG1	ILE	430	14.839	32.390	12.589	1.00	35.30
ATOM	3304	CD1	ILE	430	14.669	33.866	12.310	1.00	34.88
ATOM	3305	C	ILE	430	15.872	30.254	15.591	1.00	37.06
ATOM	3306	O	ILE	430	15.044	30.399	16.495	1.00	38.13
ATOM	3307	N	THR	431	17.109	29.823	15.808	1.00	36.61
ATOM	3308	CA	THR	431	17.600	29.520	17.146	1.00	36.17
ATOM	3309	CB	THR	431	18.067	28.053	17.240	1.00	36.58
ATOM	3310	OG1	THR	431	16.950	27.180	17.031	1.00	36.34
ATOM	3311	CG2	THR	431	18.692	27.774	18.604	1.00	36.38
ATOM	3312	C	THR	431	18.796	30.441	17.396	1.00	36.13
ATOM	3313	O	THR	431	19.705	30.513	16.569	1.00	36.10
ATOM	3314	N	PHE	432	18.804	31.157	18.514	1.00	35.79
ATOM	3315	CA	PHE	432	19.926	32.054	18.794	1.00	35.93
ATOM	3316	CB	PHE	432	19.443	33.450	19.232	1.00	34.31
ATOM	3317	CG	PHE	432	18.643	34.194	18.188	1.00	32.53
ATOM	3318	CD1	PHE	432	17.271	33.977	18.048	1.00	31.59
ATOM	3319	CD2	PHE	432	19.262	35.124	17.353	1.00	31.00
ATOM	3320	CE1	PHE	432	16.527	34.676	17.092	1.00	30.53
ATOM	3321	CE2	PHE	432	18.525	35.826	16.395	1.00	30.25
ATOM	3322	CZ	PHE	432	17.154	35.600	16.266	1.00	30.11
ATOM	3323	C	PHE	432	20.767	31.483	19.917	1.00	37.08
ATOM	3324	O	PHE	432	20.248	30.772	20.779	1.00	38.85
ATOM	3325	N	ILE	433	22.063	31.774	19.906	1.00	37.32
ATOM	3326	CA	ILE	433	22.933	31.321	20.983	1.00	38.46
ATOM	3327	CB	ILE	433	23.526	29.890	20.722	1.00	39.06
ATOM	3328	CG2	ILE	433	22.398	28.863	20.624	1.00	38.62
ATOM	3329	CG1	ILE	433	24.367	29.861	19.449	1.00	39.03
ATOM	3330	CD1	ILE	433	25.028	28.520	19.227	1.00	38.32
ATOM	3331	C	ILE	433	24.039	32.358	21.161	1.00	39.33
ATOM	3332	O	ILE	433	24.429	33.034	20.201	1.00	39.15
ATOM	3333	N	GLU	434	24.527	32.505	22.388	1.00	40.58
ATOM	3334	CA	GLU	434	25.559	33.498	22.669	1.00	42.92
ATOM	3335	CB	GLU	434	25.152	34.312	23.885	1.00	43.91
ATOM	3336	CG	GLU	434	23.769	34.883	23.744	1.00	45.53
ATOM	3337	CD	GLU	434	23.342	35.640	24.965	1.00	46.68
ATOM	3338	OE1	GLU	434	23.436	35.072	26.074	1.00	47.18
ATOM	3339	OE2	GLU	434	22.910	36.802	24.816	1.00	48.77
ATOM	3340	C	GLU	434	26.965	32.950	22.865	1.00	44.01
ATOM	3341	O	GLU	434	27.206	32.058	23.680	1.00	44.48
ATOM	3342	N	SER	435	27.901	33.518	22.119	1.00	45.00
ATOM	3343	CA	SER	435	29.284	33.075	22.167	1.00	46.11
ATOM	3344	CB	SER	435	30.077	33.779	21.057	1.00	46.95
ATOM	3345	OG	SER	435	29.839	35.186	21.053	1.00	47.94
ATOM	3346	C	SER	435	29.984	33.274	23.507	1.00	46.36
ATOM	3347	O	SER	435	30.043	34.396	24.022	1.00	46.31
ATOM	3348	N	GLU	436	30.505	32.180	24.069	1.00	46.22
ATOM	3349	CA	GLU	436	31.248	32.250	25.330	1.00	46.33
ATOM	3350	CB	GLU	436	31.322	30.884	26.020	1.00	47.64
ATOM	3351	CG	GLU	436	32.144	30.908	27.317	1.00	50.83
ATOM	3352	CD	GLU	436	32.726	29.541	27.711	1.00	52.03
ATOM	3353	OE1	GLU	436	31.951	28.585	27.970	1.00	52.84
ATOM	3354	OE2	GLU	436	33.972	29.428	27.765	1.00	52.07
ATOM	3355	C	GLU	436	32.650	32.671	24.912	1.00	45.58
ATOM	3356	O	GLU	436	33.446	31.843	24.463	1.00	45.50
ATOM	3357	N	GLU	437	32.950	33.956	25.051	1.00	44.67
ATOM	3358	CA	GLU	437	34.252	34.462	24.643	1.00	44.13

Figure 4

ATOM	3359	CB	GLU	437	35.328	34.050	25.652	1.00	43.61
ATOM	3360	CG	GLU	437	36.745	34.334	25.190	1.00	43.39
ATOM	3361	CD	GLU	437	36.931	35.752	24.678	1.00	43.50
ATOM	3362	OE1	GLU	437	36.976	36.680	25.514	1.00	44.49
ATOM	3363	OE2	GLU	437	37.025	35.940	23.441	1.00	42.17
ATOM	3364	C	GLU	437	34.569	33.880	23.264	1.00	43.56
ATOM	3365	O	GLU	437	35.530	33.131	23.108	1.00	45.30
ATOM	3366	N	GLY	438	33.757	34.225	22.266	1.00	41.68
ATOM	3367	CA	GLY	438	33.958	33.700	20.926	1.00	39.44
ATOM	3368	C	GLY	438	34.748	34.538	19.934	1.00	38.11
ATOM	3369	O	GLY	438	34.932	34.130	18.791	1.00	37.45
ATOM	3370	N	SER	439	35.213	35.713	20.329	1.00	37.14
ATOM	3371	CA	SER	439	35.980	36.502	19.386	1.00	36.86
ATOM	3372	CB	SER	439	35.916	37.983	19.714	1.00	36.81
ATOM	3373	OG	SER	439	36.825	38.678	18.878	1.00	35.32
ATOM	3374	C	SER	439	37.420	36.053	19.444	1.00	36.74
ATOM	3375	O	SER	439	38.192	36.265	18.513	1.00	36.37
ATOM	3376	N	GLY	440	37.774	35.439	20.562	1.00	36.58
ATOM	3377	CA	GLY	440	39.126	34.957	20.746	1.00	36.42
ATOM	3378	C	GLY	440	39.207	33.518	20.302	1.00	36.28
ATOM	3379	O	GLY	440	40.146	33.140	19.613	1.00	36.20
ATOM	3380	N	ARG	441	38.224	32.714	20.699	1.00	36.09
ATOM	3381	CA	ARG	441	38.190	31.309	20.312	1.00	37.16
ATOM	3382	CB	ARG	441	37.151	30.562	21.138	1.00	37.34
ATOM	3383	CG	ARG	441	37.312	30.717	22.632	1.00	39.57
ATOM	3384	CD	ARG	441	36.334	29.806	23.375	1.00	42.28
ATOM	3385	NE	ARG	441	35.270	29.339	22.488	1.00	44.36
ATOM	3386	CZ	ARG	441	34.240	28.585	22.862	1.00	45.80
ATOM	3387	NH1	ARG	441	34.103	28.192	24.127	1.00	45.87
ATOM	3388	NH2	ARG	441	33.346	28.214	21.955	1.00	47.26
ATOM	3389	C	ARG	441	37.848	31.179	18.821	1.00	37.42
ATOM	3390	O	ARG	441	38.103	30.151	18.189	1.00	37.52
ATOM	3391	N	GLY	442	37.270	32.234	18.262	1.00	37.34
ATOM	3392	CA	GLY	442	36.906	32.204	16.863	1.00	37.39
ATOM	3393	C	GLY	442	38.165	32.308	16.048	1.00	37.47
ATOM	3394	O	GLY	442	38.483	31.410	15.278	1.00	37.51
ATOM	3395	N	ALA	443	38.887	33.408	16.241	1.00	38.17
ATOM	3396	CA	ALA	443	40.134	33.660	15.526	1.00	38.50
ATOM	3397	CB	ALA	443	40.739	34.999	15.967	1.00	36.50
ATOM	3398	C	ALA	443	41.127	32.521	15.759	1.00	39.03
ATOM	3399	O	ALA	443	42.015	32.297	14.941	1.00	39.36
ATOM	3400	N	ALA	444	40.977	31.807	16.875	1.00	39.93
ATOM	3401	CA	ALA	444	41.864	30.685	17.172	1.00	40.31
ATOM	3402	CB	ALA	444	41.724	30.242	18.623	1.00	39.25
ATOM	3403	C	ALA	444	41.427	29.569	16.246	1.00	40.97
ATOM	3404	O	ALA	444	42.146	29.210	15.312	1.00	41.31
ATOM	3405	N	LEU	445	40.233	29.038	16.501	1.00	41.41
ATOM	3406	CA	LEU	445	39.678	27.960	15.690	1.00	41.97
ATOM	3407	CB	LEU	445	38.195	27.776	16.024	1.00	40.09
ATOM	3408	CG	LEU	445	37.954	26.806	17.182	1.00	39.14
ATOM	3409	CD1	LEU	445	36.750	27.233	17.982	1.00	39.27
ATOM	3410	CD2	LEU	445	37.781	25.399	16.647	1.00	37.36
ATOM	3411	C	LEU	445	39.860	28.156	14.176	1.00	43.29
ATOM	3412	O	LEU	445	39.918	27.179	13.427	1.00	43.28
ATOM	3413	N	VAL	446	39.955	29.406	13.729	1.00	44.66
ATOM	3414	CA	VAL	446	40.136	29.684	12.307	1.00	46.32
ATOM	3415	CB	VAL	446	39.687	31.120	11.948	1.00	46.15
ATOM	3416	CG1	VAL	446	40.356	31.578	10.653	1.00	46.15
ATOM	3417	CG2	VAL	446	38.164	31.160	11.793	1.00	45.75

Figure 4

```
ATOM   3418  C   VAL   446      41.597  29.503  11.944  1.00 48.03
ATOM   3419  O   VAL   446      41.929  29.105  10.825  1.00 48.75
ATOM   3420  N   SER   447      42.465  29.802  12.904  1.00 49.63
ATOM   3421  CA  SER   447      43.902  29.657  12.725  1.00 50.76
ATOM   3422  CB  SER   447      44.635  30.267  13.918  1.00 50.76
ATOM   3423  OG  SER   447      44.377  31.659  14.021  1.00 50.83
ATOM   3424  C   SER   447      44.259  28.173  12.612  1.00 52.07
ATOM   3425  O   SER   447      44.923  27.753  11.662  1.00 52.17
ATOM   3426  N   ALA   448      43.804  27.387  13.584  1.00 53.51
ATOM   3427  CA  ALA   448      44.071  25.953  13.621  1.00 55.46
ATOM   3428  CB  ALA   448      43.273  25.306  14.745  1.00 55.02
ATOM   3429  C   ALA   448      43.751  25.263  12.300  1.00 57.02
ATOM   3430  O   ALA   448      44.599  24.564  11.726  1.00 57.18
ATOM   3431  N   VAL   449      42.523  25.457  11.825  1.00 58.39
ATOM   3432  CA  VAL   449      42.093  24.841  10.579  1.00 59.69
ATOM   3433  CB  VAL   449      40.571  24.977  10.382  1.00 59.67
ATOM   3434  CG1 VAL   449      40.152  24.262   9.112  1.00 60.28
ATOM   3435  CG2 VAL   449      39.833  24.384  11.577  1.00 59.48
ATOM   3436  C   VAL   449      42.821  25.482   9.403  1.00 60.70
ATOM   3437  O   VAL   449      42.903  24.898   8.321  1.00 61.00
ATOM   3438  N   ALA   450      43.361  26.677   9.627  1.00 61.41
ATOM   3439  CA  ALA   450      44.093  27.392   8.591  1.00 62.12
ATOM   3440  CB  ALA   450      43.981  28.889   8.814  1.00 62.32
ATOM   3441  C   ALA   450      45.558  26.973   8.606  1.00 63.02
ATOM   3442  O   ALA   450      46.437  27.748   8.217  1.00 62.75
ATOM   3443  N   CYS   451      45.807  25.744   9.061  1.00 64.03
ATOM   3444  CA  CYS   451      47.160  25.183   9.148  1.00 65.19
ATOM   3445  CB  CYS   451      47.530  24.440   7.850  1.00 65.75
ATOM   3446  SG  CYS   451      46.901  22.720   7.723  1.00 66.86
ATOM   3447  C   CYS   451      48.239  26.217   9.474  1.00 65.22
ATOM   3448  O   CYS   451      47.929  27.230  10.144  1.00 65.18
ATOM   3449  OXT CYS   451      49.398  25.979   9.073  1.00 65.50
ATOM   3450  C1  HEX     1      31.023  47.521  12.611  1.00 25.83
ATOM   3451  C2  HEX     1      32.239  47.182  11.801  1.00 25.25
ATOM   3452  C3  HEX     1      32.203  45.697  11.565  1.00 25.11
ATOM   3453  C4  HEX     1      32.071  44.939  12.862  1.00 24.99
ATOM   3454  C5  HEX     1      31.030  45.591  13.785  1.00 25.34
ATOM   3455  C6  HEX     1      30.772  44.921  15.126  1.00 25.58
ATOM   3456  O1  HEX     1      30.750  48.942  12.579  1.00 27.04
ATOM   3457  O2  HEX     1      32.183  47.912  10.609  1.00 24.71
ATOM   3458  O3  HEX     1      33.337  45.251  10.836  1.00 25.99
ATOM   3459  O4  HEX     1      31.699  43.621  12.545  1.00 25.85
ATOM   3460  O5  HEX     1      31.267  46.968  13.935  1.00 25.37
ATOM   3461  O6  HEX     1      31.835  45.222  16.009  1.00 27.23
ATOM   3462  C1  LIG     1      30.034  26.620   8.669  1.00 35.87
ATOM   3463  C2  LIG     1      29.909  27.259  10.064  1.00 34.82
ATOM   3464  C3  LIG     1      31.308  27.852  10.344  1.00 35.54
ATOM   3465  C4  LIG     1      32.212  27.447   9.148  1.00 35.52
ATOM   3466  C5  LIG     1      31.520  26.207   8.584  1.00 35.20
ATOM   3467  C6  LIG     1      33.670  27.245   9.637  1.00 36.33
ATOM   3468  C7  LIG     1      34.562  26.321   8.758  1.00 37.11
ATOM   3469  C8  LIG     1      35.946  26.832   8.778  1.00 36.91
ATOM   3470  N9  LIG     1      36.382  27.317   7.570  1.00 36.92
ATOM   3471  C10 LIG     1      37.668  27.907   7.331  1.00 36.42
ATOM   3472  N11 LIG     1      38.035  28.336   6.087  1.00 37.39
ATOM   3473  C12 LIG     1      39.058  28.930   6.462  1.00 36.99
ATOM   3474  C13 LIG     1      39.426  29.003   7.575  1.00 37.10
ATOM   3475  S14 LIG     1      38.681  28.342   8.700  1.00 37.86
ATOM   3476  O15 LIG     1      36.640  26.843   9.817  1.00 38.32
```

Figure 4


```
ATOM   3477  C16 LIG     1      34.538  24.890   9.296  1.00 37.59
ATOM   3478  C17 LIG     1      34.906  24.620  10.610  1.00 37.22
ATOM   3479  C18 LIG     1      34.658  23.346  11.130  1.00 38.09
ATOM   3480  N19 LIG     1      34.084  22.371  10.404  1.00 38.80
ATOM   3481  C20 LIG     1      33.729  22.598   9.128  1.00 38.90
ATOM   3482  C21 LIG     1      33.942  23.860   8.546  1.00 38.73
ATOM   3483  K1  K       1      32.471  32.037  -7.104  1.00 46.91
END
```

CRYSTALS OF GLUCOKINASE AND METHODS OF GROWING THEM

The invention relates to crystalline forms of Glucokinase of sufficient size and quality to obtain structural data by X-ray crystallography and to methods of growing such crystals.

Glucokinase (GK) is one of four hexokinases found in mammals [Colowick, S.P., in *The Enzymes*, Vol. 9 (P. Boyer, ed.) Academic Press, New York, NY, pages 1-48, 1973]. The hexokinases catalyze the first step in the metabolism of glucose, i.e., the conversion of glucose to glucose-6-phosphate. Glucokinase has a limited cellular distribution, being found principally in pancreatic β-cells and liver parenchymal cells. In addition, GK is a rate-controlling enzyme for glucose metabolism in these two cell types that are known to play critical roles in whole-body glucose homeostasis [Chipkin, S.R., Kelly, K.L., and Ruderman, N.B. in *Joslin's Diabetes* (C.R. Khan and G.C. Wier, eds.), Lea and Febiger, Philadelphia, PA, pages 97-115, 1994]. The concentration of glucose at which GK demonstrates half-maximal activity is approximately 8 mM. The other three hexokinases are saturated with glucose at much lower concentrations (<1 mM). Therefore, the flux of glucose through the GK pathway rises as the concentration of glucose in the blood increases from fasting (5 mM) to postprandial (≈10-15 mM) levels following a carbohydrate-containing meal [Printz, R.G., Magnuson, M.A., and Granner, D.K. in *Ann. Rev. Nutrition* Vol. 13 (R.E. Olson, D.M. Bier, and D.B. McCormick, eds.), Annual Review, Inc., Palo Alto, CA, pages 463-496, 1993]. These findings contributed over a decade ago to the hypothesis that GK functions as a glucose sensor in β-cells and hepatocytes (Meglasson, M.D. and Matschinsky, F.M. *Amer. J. Physiol.* **246**, E1-E13, 1984). In recent years, studies in transgenic animals have confirmed that GK does indeed play a critical role in whole-body glucose homeostasis. Animals that do not express GK die within days of birth with severe diabetes while animals overexpressing GK have improved glucose tolerance (Grupe, A., Hultgren, B., Ryan, A. et al., *Cell* **83**, 69-78, 1995; Ferrie, T., Riu, E., Bosch, F. et al., *FASEB J.*, **10**, 1213-1218, 1996). An increase in glucose exposure is coupled through GK in β-cells to increased insulin secretion and in hepatocytes to increased glycogen deposition and perhaps decreased glucose production.

The finding that type II maturity-onset diabetes of the young (MODY-2) is caused by loss of function mutations in the GK gene suggests that GK also functions as a glucose sensor in humans (Liang, Y., Kesavan, P., Wang, L. et al., *Biochem. J.* 309, 167-173, 1995). Additional evidence supporting an important role for GK in the regulation of glucose metabolism in humans was provided by the identification of patients that express a mutant form of GK with increased enzymatic activity. These patients exhibit a fasting hypoglycemia associated with an inappropriately elevated level of plasma insulin (Glaser, B., Kesavan, P., Heyman, M. et al., *New England J. Med.* 338, 226-230, 1998). While mutations of the GK gene are not found in the majority of patients with type II diabetes, compounds that activate GK and, thereby, increase the sensitivity of the GK sensor system will still be useful in the treatment of the hyperglycemia characteristic of all type II diabetes. Glucokinase activators will increase the flux of glucose metabolism in β-cells and hepatocytes, which will be coupled to increased insulin secretion. Such agents would be useful for treating type II diabetes.

In an effort to elucidate the mechanisms underlying kinase activation , the crystal structure of such proteins is often sought to be determined. The crystal structures of several hexokinases have been reported. See, e.g. A. E. Aleshin, C. Zeng, G. P. Bourenkov, H. D. Bartunik, H. J. Fromm & R. B. Honzatko 'The mechanism of regulation of hexokinase: new insights from the crystal structure of recombinant human brain hexokinase complexed with glucose and glucose-6-phosphate' *Structure* 6, 39-50 (1998); W. S. Bennett, Jr. & T. A. Steitz 'Structure of a complex between yeast hexokinase A and glucose I. Structure determination and refinement at 3.5 Å resolution' *J. Mol. Biol.* 140, 183-209 (1978); and S. Ito, S. Fushinobu, I. Yoshioka, S. Koga, H. Matsuzawa & T. Wakagi 'Structural Basis for the ADP-Specificity of a Novel Glucokinase from a Hyperthermophilic Archaeon' *Structure* 9, 205-214 (2001). Despite these reports, researchers armed with the knowledge of how to obtain crystals of related hexokinases have attempted to obtain crystals of any mammalian Glucokinase without success.

Applicants have discovered protocols which allow crystallization of mammalian Glucokinase with or without a bound allosteric ligand. The crystal structure has been solved by X-ray crystallography to a resolution of 2.7 Å. See Figures 3 and 4. Thus the invention relates to a crystalline form of Glucokinase and a crystalline form of a complex of Glucokinase and an allosteric ligand. The invention further relates to a method of forming crystals of Glucokinase, with or without a bound allosteric ligand.

Figure 1 shows Glucokinase co-crystals having P6(5)22 symmetry.

Figure 2 shows the amino acid sequence of an expressed Glucokinase used for crystallization.

Figure 3 shows a ribbon diagram of the structure of Glucokinase showing the α-helices and β-sheets.

Figure 4 shows the atomic structure coordinates for Glucokinase bound to 3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide.

The present invention relates to crystalline forms of mammalian Glucokinase, with or without a ligand bound in the allosteric site, where the crystals are of sufficient quality and size to allow for the determination of the three-dimensional X-ray diffraction structure to a resolution of about 2.0 Å to about 3.5 Å. The invention also relates to methods for preparing and crystallizing the Glucokinase. The crystalline forms of Glucokinase, as well as information derived from their crystal structures can be used to analyze and modify glucokinase activity as well as to identify compounds that interact with the allosteric site.

The crystals of the invention include apo crystals and co-crystals. The apo crystals of the invention generally comprise substantially pure Glucokinase. The co-crystals generally comprise substantially pure Glucokinase with a ligand bound to the allosteric site.

It is to be understood that the crystalline Glucokinases of the invention are not limited to naturally occurring or native Glucokinases. Indeed, the crystals of the invention include mutants of the native Glucokinases. Mutants of native Glucokinases are obtained by replacing at least one amino acid residue in a native Glucokinase domain with a different amino acid residue, or by adding or deleting amino acid residues within the native polypeptide or at the N- or C- terminus of the native polypeptide, and have substantially the same three-dimensional structure as the native Glucokinase from which the mutant is derived.

By having substantially the same three-dimensional structure is meant having a set of atomic structure coordinates from an apo- or co-crystal that have a root mean square deviation of less than or equal to about 2 Å when superimposed with the atomic structure coordinates of the native Glucokinase from which the mutant is derived when at least about 50% to about 100% of the alpha carbon atoms of the native Glucokinase are included in the superposition.

In some instances, it may be particularly advantageous or convenient to substitute, delete and/or add amino acid residues to a native Glucokinase domain in order to provide convenient cloning sites in cDNA encoding the polypeptide, to aid in purification of the polypeptide, etc. Such substitutions, deletions and/or additions which do not substantially alter the three dimensional structure of the native Glucokinase will be apparent to those having skills in the art.

It should be noted that the mutants contemplated herein need not exhibit glucokinase activity. Indeed, amino acid substitutions, additions or deletions that interfere with the kinase activity of the glucokinase but which do not significantly alter the three-dimensional structure of the domain are specifically contemplated by the invention. Such crystalline polypeptides, or the atomic structure coordinates obtained therefrom, can be used to identify compounds that bind to the native domain. These compounds may affect the activity or the native domain.

The derivative crystals of the invention generally comprise a crystalline glucokinase polypeptide in covalent association with one or more heavy metal atoms. The polypeptide may correspond to a native or a mutated Glucokinase. Heavy metal atoms useful for providing derivative crystals include, by way of example and not limitation, gold and mercury. Alternatively, derivative crystals can be formed from proteins which have heavy atoms incorporated into one or more amino acids, such as seleno-methionine substitutions for methionine.

The co-crystals of the invention generally comprise a crystalline Glucokinase polypeptide in association with one or more compounds at an allosteric site of the polypeptide. The association may be covalent or non-covalent.

The native and mutated glucokinase polypeptides described herein may be isolated from natural sources or produced by methods well known to those skilled in the art of molecular biology. Expression vectors to be used may contain a native or mutated Glucokinase polypeptide coding sequence and appropriate transcriptional and/or translational control signals. These methods include in vitro recombinant DNA techniques, synthetic techniques and in vivo recombination/genetic recombination. See, for example, the techniques described in Maniatis et al., 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, NY; and Ausubel et al., 1989, *Current Protocols in Molecular Biology*, Greene Publishing Associates and Wiley Interscience, NY.

A variety of host-expression vector systems may be utilized to express the Glucokinase coding sequence. These include but are not limited to microorganisms such as bacteria transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing the Glucokinase coding sequence; yeast transformed with recombinant yeast expression vectors containing the Glucokinase coding sequence; insect cell systems infected with recombinant virus expression vectors (e.g. baculovirus) containing the Glucokinase coding sequence; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosiac virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing the glucokinase coding sequence; or animal cell systems. The expression elements of these systems vary in their strength and specificities. Depending on the host/vector system utilized, any of a number of suitable transcription and translation elements, including constitutive and inducible promotors such as pL of bacteriophage μ, plac, ptrp, ptac (ptrp-lac hybrid promoter) and the like may be used; when cloning in insect cell systems, promoters such as the baculovirus polyhedrin promoter may be used; when cloning in plant cell systems, promoters derived from the genome of plant cells (e.g., heat shock promoters; the promoter for the small subunit of RUBISCO; the promoter for the chlorophyll a/b binding protein) or from plant viruses (e.g., the 35 S RNA promoter of CaMV; the coat protein promoter of TMV) may be used; when cloning in mammalian cell systems, promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter) may be used; when generating cell lines that contain multiple copies of the glucokinase coding sequence, SV40-, BPV- and EBV-based vectors may be used with an appropriate selectable marker.

The apo, derivative and co-crystals of the invention can be obtained by techniques well-known in the art of protein crystallography, including batch, liquid bridge, dialysis, vapor diffusion and hanging drop methods (see e.g. McPherson, 1982, *Preparation and Analysis of Protein Crystals*, John Wiley, NY; McPherson, 1990, *Eur. J. Biochem.* 189:1-23; Webber, 1991, *Adv. Protein Chem.* 41:1-36; Crystallization of Nucleic Acids and Proteins, Edited by Arnaud Ducruix and Richard Giege, Oxford University Press; Protein Crystallization Techniques, Strategies, and Tips, Edited by Terese Bergfors, International University Line, 1999). Generally, the apo- or co-crystals of the invention are grown by

placing a substantially pure Glucokinase polypeptide in an aqueous buffer containing a precipitant at a concentration just below that necessary to precipitate the protein. Water is then removed from the solution by controlled evaporation to produce crystallizing conditions, which are maintained until crystal growth ceases.

In a preferred embodiment of the invention, apo or co-crystals are grown by vapor diffusion. In this method, the polypeptide/precipitant solution is allowed to equilibrate in a closed container with a larger aqueous reservoir having a precipitant concentration optimal for producing crystals. Generally, less than about 10 µL of subtantially pure polypeptide solution is mixed with an equal volume of reservoir solution, giving a precipitant concentration about half that required for crystallization. This solution is suspended as a droplet underneath a coverslip, which is sealed onto the top of a reservoir. The sealed container is allowed to stand, from one day to one year, usually for about 2-6 weeks, until crystals grow.

For crystals of the invention, it has been found that hanging drops containing about 2-5 µl of Glucokinase (9-22 mg/ml in 20 mM tris pH 7.1 measured at room temperature, 50 mM NaCl, 50 mM glucose, 10 mM DTT and optionally 0.2 mM EDTA) and an equal amount of reservoir solution (16-25% w/v polyethylene glycol with an average molecular weight from about 8000 to about 10000 Daltons, 0.1-0.2 M tris or bistris or Hepes or ammonium phosphate buffer, pH 6.9-7.5, 8-10 mM DTT, 0 - 30% saturated glucose) suspended over 0.5 to 1.0 mL reservoir buffer for about 3-4 weeks at 4-6°C provided crystals suitable for high resolution X-ray structure determination. Particularly preferred conditions were: about 2-5 µl of Glucokinase (10 mg/ml in 20 mM tris pH 7.1 measured at room temperature, 50 mM NaCl, 50 mM glucose, 10 mM DTT and optionally 0.2 mM EDTA) and an equal amount of reservoir solution (22.5% w/v polyethylene glycol with an average molecular weight of about 10000 Daltons, 0.1 M tris pH 7.08, 10 mM DTT, 20% glucose) were suspended over 0.5 to 1.0 mL reservoir buffer for about 3-4 weeks at 4-6°C.

The optimum procedure for growing crystals large enough to collect data from involved first streaking 3-4 µl of protein solution on the coverslip, followed by streaking 3-4 µl of well solution across the elongated droplet of protein, forming a droplet shaped like the letter 'X'. Before discovering this crossed droplet technique, most droplets yielded showers of small crystals which were not large enough for data collection purposes. The crossed droplets allow gradients of protein and precipitating agent to form as the two solutions slowly mix, and the resulting kinetics of crystal nucleation and growth are optimal for the growth of a small number of large crystals in each crossed droplet. Simply mixing the protein and precipitant solutions together in a single round droplet often produced an overabundance of nuclei which grew to a final size too small for data collection purposes. Crystals usually appeared within 5 days of setup. The crystals grow in the form of hexagonal bipyramids, reaching dimensions of 0.2 x 0.2 x 0.4 mm typically, although larger crystals are often observed. Figure 1 shows grown crystals.

Crystals may be frozen prior to data collection. The crystals were cryo-protected with either (a) 20-30% saturated glucose present in the crystallization setup, (b) ethanol added to 15-20%, (c) ethylene glycol added to 10-20% and PEG10,000 brought up to 25%, or (d) glycerol added to 15%. The crystals were either briefly immersed in the cryo-protectant or soaked in the cryo-protectant for periods as long as a day. Freezing was accomplished by immersing the crystal in a bath of liquid nitrogen or by placing the crystal in a stream of nitrogen gas at 100 K.

The mosaic spread of the frozen crystals could sometimes be reduced by annealing, wherein the stream of cold nitrogen gas is briefly blocked, allowing the frozen crystal to thaw momentarily before re-freezing in the nitrogen gas stream. Another technique which was sometimes helpful in data collection was to center one of the ends of the hexagonal bipyramid in the x-ray beam, rather than the mid portion of the crystal. The mosaic spread could sometimes be reduced by this technique.

Diffraction data typically extending to 2.7 Å was collected from the frozen crystals at the synchrotron beamline X8C of the National Synchrotron Light Source in Brookhaven, New York. Under optimum conditions, data extending to 2.2 Å was recorded. See Figures 3 and 4 for solution. The space group of the crystals was determined to be P6(5)22 during the course of the solution of the crystal structure. The crystals have unit cell dimensions a = b = 79.62 +/- 0.60 Å, c = 321.73 +/- 3.70 Å, $\alpha\gamma = \beta = 90°$, $\gamma = 120°$. The crystals are in a hexagonal system with P6(5)22 symmetry.

Of course, those having skill in the art will recognize that the above-described crystallization conditions can be varied. Such variations may be used alone or in combination, and include polypeptide solutions containing polypeptide concentrations between 1 mg/mL and 60 mg/mL, any commercially available buffer systems which can maintain pH from about 6.5 to about 7.6, Tris-HCl concentrations between 10 mM and 200 mM, dithiothreitol concentrations between 0 mM and 20 mM, preferably between 8 and 10 mM, substitution of dithiothreitol with beta mercapto ethanol or other art-recognized equivalents, glucose concentrations between 0% w/v and 30% w/v, or substitution of glucose with other sugars known to bind to Glucokinase; and reservoir solutions containing polyethylene glycol (PEG) concentrations between about 10% and about 30%, polyethylene glycol average molecular weights between about 1000 and about 20,000 daltons, any commercially available buffer systems which can maintain pH from about 6.5 to about 7.6, dithiothreitol concentrations between 0 mM and 20 mM, substitution of dithiothreitol with beta mercapto ethanol or other art-recognized -SH group containing equivalents, or substitution of glucose with other sugars known to bind to Glucokinase, and temperature ranges between 4 and 20°C.

Derivative crystals of the invention can be obtained by soaking apo or co-crystals in mother liquor containing salts of heavy metal atoms, according to procedures known to those of skill in the art of X-ray crystallography.

Co-crystals of the invention can be obtained by soaking an apo crystal in mother liquor containing a ligand that binds to the allosteric site, or can be obtained by co-crystallizing the Glucokinase polypeptide in the presence of one or more ligands that bind to the allosteric site. Preferably, co-crystals are formed with a glucokinase activator disclosed in US Pat. No. 6,320,050; US Pat. Appl. 09/532,506 filed March 21, 2000; US Pat. Appl. 09/675,781 filed September 28, 2000; US Pat. Appl. 09/727,624, filed December 1, 2000; US Pat. Appl. 09/841,983, filed April 25, 2001; US Pat. Appl. 09/843,466, filed April 26, 2001; US Pat. Appl. 09/846,820, filed May 1, 2001; US Pat. Appl. 09/846,821, filed May 1, 2001; US Pat. Appl. 09/905,152, filed July 13, 2001; US Pat. Appl. 09/924,247, filed August 8, 2001; US Provisional Pat. Appl. 60/251,637, filed December 6, 2000; or US Provisional Pat. Appl. 60/318,715, filed September 13, 2001, each of which is incorporated herein by reference.

Methods for obtaining the three-dimensional structure of the crystalline glucokinases described herein, as well as the atomic structure coordinates, are well-known in the art (see, e.g., D. E. McRee, Practical Protein Crystallography, published by Academic Press, San Diego (1993), and references cited therein).

The crystals of the invention, and particularly the atomic structure coordinates obtained therefrom, have a wide variety of uses. For example, the crystals and structure coordinates described herein are particularly useful for identifying compounds that activate Glucokinases as an approach towards developing new therapeutic agents. One such compound is 3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide and pharmaceutically acceptable salts thereof. Pharmaceutical compositions of said compounds can be developed, and said compounds can be used for the manufacture of a medicament comprising said compound for the treatment of hyperglycemia in type II diabetes.

The structure coordinates described herein can be used as phasing models in determining the crystal structures of additional native or mutated glucokinases, as well as

the structures of co-crystals of such glucokinases with allosteric inhibitors or activators bound. The structure coordinates, as well as models of the three-dimensional structures obtained therefrom, can also be used to aid the elucidation of solution-based structures of native or mutated glucokinases, such as those obtained via NMR. Thus, the crystals and atomic structure coordinates of the invention provide a convenient means for elucidating the structures and functions of glucokinases.

For purposes of clarity and discussion, the crystals of the invention will be described by reference to specific Glucokinase exemplary apo crystals and co-crystals. Those skilled in the art will appreciate that the principles described herein are generally applicable to crystals of any mammalian Glucokinase, including, but not limited to the Glucokinase of Figure 2.

As used herein, "allosteric site" refers in general to any ligand binding site on a mammalian Glucokinase other than the active site of the enzyme.

As used herein, "apo crystal" refers to crystals of mammalian Glucokinase formed without a bound allosteric ligand.

As used herein, "allosteric ligand" refers to any molecule which specifically binds an allosteric site on a mammalian Glucokinase.

EXAMPLES

Example 1: Expression and Purification of Glucokinase

Expression of GK

Glucokinase (GK) was expressed as a glutathione S-transferase (GST) fusion protein in *Escherichia coli*. The amino-acid sequence of the fusion protein is given in Figure 2. The expression construct is based on the pGEX-3X vector from Pharmacia, as described in Y. Liang, P. Kesavan, L. Wang, K. Niswender, Y. Tanizawa, M. A. Permutt, M. A. Magnuson, F. M. Matschinsky, *Biochem. J.* 309, 167 (1995). The construct codes for one of the two liver isozymes of human GK. The GST tag is at the N-terminus of the construct, and is separated from the coding sequence for GK by a Factor Xa cleavage site. After purification of the GST fusion protein, the GST fusion tag was removed with Factor Xa protease, which also removes five residues from the N-terminus of GK.

Purification of GK

E. coli cells expressing GST-GK were suspended in lysis buffer (50 mM tris, 200 mM NaCl, 5 mM EDTA, 5 mM DTT, 1% NP-40, pH 7.7) in the presence of protease inhibitors, incubated with lysozyme at 200 μ/ml for 30 minutes at room temperature, and sonicated 4x30 sec. at 4° C. After centrifugation to remove insoluble material, the supernatant was loaded onto glutathione-Sepharose, washed with lysis buffer and then with lysis buffer minus NP-40. GST-GK was eluted with lysis buffer (minus NP-40) containing 50 mM D-glucose and 20 mM glutathione. The eluted protein was concentrated and dialyzed into 20 mM tris, 100 mM NaCl, 0.2 mM EDTA, 50 mM D-glucose, 1mM DTT, pH 7.7. Factor Xa was added at a protein ratio of 1:100 GST-GK followed by the addition of $CaCl_2$ to 1 mM, and the sample was incubated at 4° C for 48

hours. The sample was added to glutathione Sepharose and the unbound fraction collected and concentrated. The sample was then incubated with benzamidine Sepharose to remove Factor Xa, and the unbound fraction was collected and loaded on a Q Sepharose column equilibrated with 25 mM bis-tris propane, 50 mM NaCl, 5 mM DTT, 50 mM D-glucose and 5% glycerol (pH 7.0). The protein was eluted with a NaCl gradient from 50-400 mM. Fractions containing purified GK were pooled and concentrated and filtered.

Example 2: Formation of apo Crystal

4 µl of glucokinase and 4 µl of precipitant were mixed and equilibrated against the precipitant solution at 4° C. The glucokinase solution consisted of 22 mg/ml glucokinase prepared in Example 1 in 20 mM hepes pH 7.5, 50 mM NaCl, 10 mM DTT, and 50 mM glucose. The precipitant consisted of 22.5% PEG10000, 0.1 M tris pH 7.08, 10 mM DTT, 20% glucose; the precipitant solution contained seed crystals in order to microseed the droplets. Crystals appeared in the droplets after leaving the crystallization plates at 4° C.

Example 3: Formation of Co-crystal with 3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide

3(a):

4 µl of glucokinase and 4 µl of precipitant were mixed and equilibrated against the precipitant solution at 4° C. The glucokinase solution consisted of 13 mg/ml glucokinase prepared in Example 1 in 20 mM tris pH 7.0, 50 mM NaCl, 10 mM DTT, 50 mM glucose, and the glucokinase activator 3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide at a concentration 5 times that of the protein. The precipitant consisted of 22.5% PEG10000, 0.1 M tris pH 7.08, 10 mM DTT, 20% glucose. Crystals appeared in the droplets after leaving the crystallization plates at 4° C.

3(b):

Alternatively, crystals were grown as in Example 3(a) with the following changes: instead of 4 µl glucokinase and 4 µl precipitant, 2 µl of each were used; the glucokinase solution contained 11 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant 18% PEG8000 was used; the precipitant solution contained seed crystals in order to microseed the droplets.

3(c):

In another alternative, crystals were grown as in Example 3(a) with the following changes: instead of 4 µl glucokinase and 4 µl precipitant, 2 µl of each were used; the glucokinase solution contained 11 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant 20% PEG8000 was used; the precipitant solution contained seed crystals in order to microseed the droplets.

3(d):

In yet another alternative, crystals were grown as in Example 3(a) with the following changes: instead of 4 µl glucokinase and 4 µl precipitant, 2 µl of each were used; the glucokinase solution contained 12 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant 16% PEG10000 was used; glucose was not present as a component of the precipitant; the precipitant solution contained seed crystals in order to microseed the droplets.

3(e):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 11 mg/ml glucokinase in tris

buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant 25% PEG10000 was used.

3(f):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 11 mg/ml glucokinase in tris buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant 21.25% PEG10000 was used; in place of tris buffered at pH 7.08 in the precipitant tris buffered at pH 7.52 was used.

3(g):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 12 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of tris buffered at pH 7.08 in the precipitant, hepes buffered at pH 6.89 was used; in place of 20% glucose in the precipitant, 200 mM glucose was used.

3(h):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 12 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 0.1 M tris buffered at pH 7.08 in the precipitant, 0.2 M ammonium phosphate buffered at pH 7.03 was used; in place of 20% glucose in the precipitant, 200 mM glucose was used.

3(i):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 10 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant, 20% PEG10000 was used; in place of tris buffered at pH 7.08 in the precipitant, tris buffered at pH 7.05 was used; in place of 10 mM DTT in the precipitant, 8 mM DTT was used; glucose was not present as a component of the precipitant.

3(j):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 12 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 22.5% PEG10000 as precipitant, 22% PEG8000 was used; glucose was not present as a component of the precipitant; the precipitant solution contained seed crystals in order to microseed the droplets.

3(k):

In still another alternative, crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 11 mg/ml glucokinase in tris buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of 20% glucose in the precipitant, 30% glucose was used.

Example 4: Formation of Co-crystal with N-(5-Bromo-pyridin-2-yl)-2-(3-chloro-4-methanesulfonyl-phenyl)-3-cyclopentyl-propionamide

Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 9 mg/ml glucokinase in tris buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase activator of Example 3(a), the glucokinase solution contained the glucokinase activator N-(5-Bromo-pyridin-2-yl)-2-(3-chloro-4-methanesulfonyl-phenyl)-3-cyclopentyl-propionamide; in place of 20% glucose in the precipitant, 200 mM glucose was used.

Example 5: Formation of Co-crystal with 2-(3-Chloro-4-methanesulfonyl-phenyl)-3-cyclopentyl-N-(5-trifluoromethyl-pyridin-2-yl)-propionamide

Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 10 mg/ml glucokinase in tris buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase

activator of Example 3(a), the glucokinase solution contained the glucokinase activator 2-(3-Chloro-4-methanesulfonyl-phenyl)-3-cyclopentyl-N-(5-trifluoromethyl-pyridin-2-yl)-propionamide; in place of 22.5% PEG10000 as precipitant, 21.25% PEG10000 was used.

Example 6: Formation of Co-crystal with (2S)-2-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionylamino]-thiazole-4-carboxylic acid methyl ester

Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 10 mg/ml glucokinase in tris buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase activator of Example 3(a), the glucokinase solution contained the glucokinase activator (2S)-2-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionylamino]-thiazole-4-carboxylic acid methyl ester; in place of 22.5% PEG10000 as precipitant, 21.25% PEG10000 was used; in place of tris buffered at pH 7.08 in the precipitant, bistris buffered at pH 7.0 was used.

Example 7: Formation of Co-crystal with (2S)-{2-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionylamino]-thiazol-5-yl}-oxo-acetic acid ethyl ester

Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 10 mg/ml glucokinase in tris buffer at pH 7.1 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase activator of Example 3(a), the glucokinase solution contained the glucokinase activator (2S)-{2-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionylamino]-thiazol-5-yl}-oxo-acetic acid ethyl ester; in place of 22.5% PEG10000 as precipitant, 21.25% PEG10000 was used.

Example 8: Formation of Co-crystal with (2S)-{3-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionyl]-ureido}-acetic acid methylester

Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 9 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase activator of Example 3(a), the glucokinase solution contained the glucokinase activator (2S)-{3-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionyl]-ureido}-acetic acid methylester; in place of 20% glucose in the precipitant, 200 mM glucose was used.

Example 9: Formation of Co-crystal with (2S)-1-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionyl]-3-(3-hydroxy-propyl)-urea

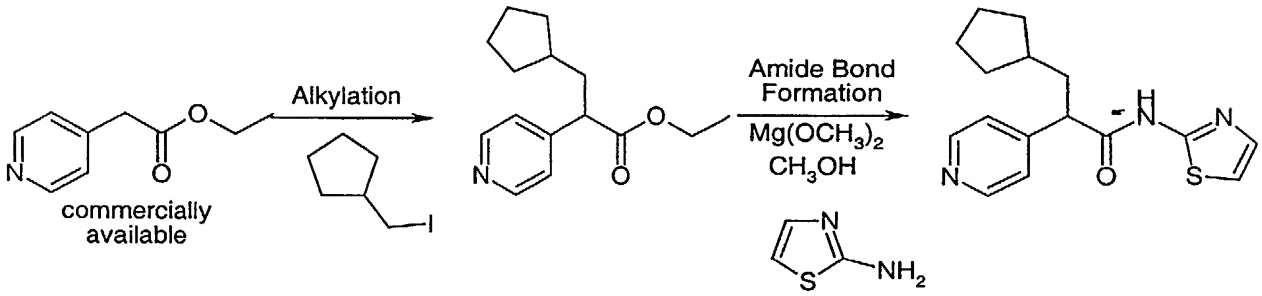
Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 14 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase activator of Example 3(a), the glucokinase solution contained the glucokinase activator (2S)-1-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionyl]-3-(3-hydroxy-propyl)-urea; in place of 20% glucose in the precipitant, 200 mM glucose was used.

Example 10: Formation of Co-crystal with (2S)-{3-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionyl]-ureido}-acetic acid ethyl ester

Crystals were grown as in Example 3(a) with the following changes: the glucokinase solution contained 14 mg/ml glucokinase in tris buffer at pH 7.08 instead of 7.0; the glucokinase solution included 0.2 mM EDTA; in place of the glucokinase activator of Example 3(a), the glucokinase solution contained the glucokinase activator (2S)-{3-[3-Cyclopentyl-2-(3,4-dichloro-phenyl)-propionyl]-ureido}-acetic acid ethyl ester; in place of tris buffered at pH 7.08 in the precipitant, tris buffered at pH 7.05 was used.

Example 11: Synthesis of 3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide

3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide can be prepared using well-



known organic synthesis techniques according to the following reaction scheme:

3-Cyclopentyl-2-pyridin-4-yl-N-thiazol-2-yl-propionamide is useful as an allosteric activator of Glucokinase and to assist the formation of co-crystals of Glucokinase.

In the present specification "comprises" means "includes or consists of" and "comprising" means "including or consisting of".

The features disclosed in the foregoing description, or the following claims, or the accompanying drawings, expressed in their specific forms or in terms of a means for performing the disclosed function, or a method or process for attaining the disclosed result, as appropriate, may, separately, or in any combination of such features, be utilised for realising the invention in diverse forms thereof.

SEQUENCE LISTING

<110> F. Hoffmann - La Roche

<120> CRYSTALS OF GLUCOKINASE AND METHODS OF GROWING THEM

<130> Case 20892

<140> US 60/341988

<141> 2001-12-19

<150> US 60/341988

<151> 2001-12-19

<160> 1

<170> PatentIn version 3.1

<210> 1

<211> 692

<212> PRT

<213> Homo sapiens

<220>

<221> GK

<222> (229)..(692)

<223>

<300>

<308> Genbank U13852

<309> 1994-12-13

<313> (1)..(228)

<400> 1

Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
1 5 10 15

Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
20 25 30

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu

35 40 45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys

50 55 60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn

65 70 75 80

Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu

85 90 95

Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser

100 105 110

Lys Asp Phe Glu Thr Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu

115 120 125

Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn

130 135 140

Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp

145 150 155 160

Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu

165 170 175

Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr

180 185 190

Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala

195 200 205

Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Ile Glu Gly

210 215 220

Arg Gly Ile His Met Pro Arg Pro Arg Ser Gln Leu Pro Gln Pro Asn

225 230 235 240

Ser Gln Val Glu Gln Ile Leu Ala Glu Phe Gln Leu Gln Glu Glu Asp

245 250 255

Leu Lys Lys Val Met Arg Arg Met Gln Lys Glu Met Asp Arg Gly Leu

260 265 270

Arg Leu Glu Thr His Glu Glu Ala Ser Val Lys Met Leu Pro Thr Tyr

275 280 285

Val Arg Ser Thr Pro Glu Gly Ser Glu Val Gly Asp Phe Leu Ser Leu

290 295 300

Asp Leu Gly Gly Thr Asn Phe Arg Val Met Leu Val Lys Val Gly Glu

305 310 315 320

Gly Glu Glu Gly Gln Trp Ser Val Lys Thr Lys His Gln Met Tyr Ser

325 330 335

Ile Pro Glu Asp Ala Met Thr Gly Thr Ala Glu Met Leu Phe Asp Tyr

340 345 350

Ile Ser Glu Cys Ile Ser Asp Phe Leu Asp Lys His Gln Met Lys His

355 360 365

Lys Lys Leu Pro Leu Gly Phe Thr Phe Ser Phe Pro Val Arg His Glu

370 375 380

Asp Ile Asp Lys Gly Ile Leu Leu Asn Trp Thr Lys Gly Phe Lys Ala

385 390 395 400

Ser Gly Ala Glu Gly Asn Asn Val Val Gly Leu Leu Arg Asp Ala Ile

405 410 415

Lys Arg Arg Gly Asp Phe Glu Met Asp Val Val Ala Met Val Asn Asp

420 425 430

Thr Val Ala Thr Met Ile Ser Cys Tyr Tyr Glu Asp His Gln Cys Glu

435 440 445

Val Gly Met Ile Val Gly Thr Gly Cys Asn Ala Cys Tyr Met Glu Glu

450 455 460

Met Gln Asn Val Glu Leu Val Glu Gly Asp Glu Gly Arg Met Cys Val

465 470 475 480

Asn Thr Glu Trp Gly Ala Phe Gly Asp Ser Gly Glu Leu Asp Glu Phe

485 490 495

Leu Leu Glu Tyr Asp Arg Leu Val Asp Glu Ser Ser Ala Asn Pro Gly

500 505 510

Gln Gln Leu Tyr Glu Lys Leu Ile Gly Gly Lys Tyr Met Gly Glu Leu

515 520 525

Val Arg Leu Val Leu Leu Arg Leu Val Asp Glu Asn Leu Leu Phe His

530 535 540

Gly Glu Ala Ser Glu Gln Leu Arg Thr Arg Gly Ala Phe Glu Thr Arg

545 550 555 560

Phe Val Ser Gln Val Glu Ser Asp Thr Gly Asp Arg Lys Gln Ile Tyr

565 570 575

Asn Ile Leu Ser Thr Leu Gly Leu Arg Pro Ser Thr Thr Asp Cys Asp

580 585 590

Ile Val Arg Arg Ala Cys Glu Ser Val Ser Thr Arg Ala Ala His Met

595 600 605

Cys Ser Ala Gly Leu Ala Gly Val Ile Asn Arg Met Arg Glu Ser Arg

610 615 620

Ser Glu Asp Val Met Arg Ile Thr Val Gly Val Asp Gly Ser Val Tyr

625 630 635 640

Lys Leu His Pro Ser Phe Lys Glu Arg Phe His Ala Ser Val Arg Arg

645 650 655

Leu Thr Pro Ser Cys Glu Ile Thr Phe Ile Glu Ser Glu Glu Gly Ser

660 665 670

Gly Arg Gly Ala Ala Leu Val Ser Ala Val Ala Cys Lys Lys Ala Cys

675 680 685

Met Leu Gly Gln

690

Claims

1. A co-crystal of mammalian Glucokinase and a ligand bound to an allosteric site of the Glucokinase, wherein

the co-crystal has unit cell dimensions of:

a and b are from 79.02 Å to 80.22 Å;

c is from 318.03 Å to 325.03 Å;

α and β are 90°; and

γ is 120°;

and the co-crystal has P6(5)22 symmetry.

2. A crystal of mammalian Glucokinase, wherein

the crystal has unit cell dimensions of:

a and b are from 79.02 Å to 80.22 Å;

c is from 318.03 Å to 325.03 Å;

α and β are 90°; and

γ is 120°;

and the crystal has P6(5)22 symmetry.

3. A process for co-crystalizing mammalian Glucokinase and an allosteric ligand of Glucokinase, the process comprising:

providing a buffered, aqueous solution of 9 to 22 mg/ml of the mammalian Glucokinase;

adding a molar excess of the allosteric ligand to the aqueous solution of mammalian Glucokinase; and

growing crystals by vapor diffusion using a buffered reservoir solution between about 10% and about 30% PEG, about 0% w/v and about 30% w/v glucose, and between 0 and 20 mM DTT, wherein the PEG has an average molecular weight between about 1,000 and about 20,000.

4. The process of claim 3, wherein the step of growing crystals by vapor diffusion comprises:

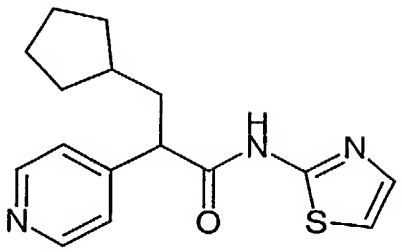
streaking the buffered, aqueous solution of mammalian Glucokinase with added allosteric ligand on a surface to form an elongated droplet of protein solution, and

streaking about an equal amount of the buffered reservoir solution across the elongated droplet of protein solution, forming a combined droplet shaped like the letter 'X'.

5. A crystal produced by the process of claims 3 or 4.

6. A compound identified by analysing the structure coordinates of the co-crystal of claim 1, said compound being a ligand that binds to the allosteric site of Glucokinase.

7. The compound



and pharmaceutically acceptable salts thereof.

8. A pharmaceutical composition comprising the compound of claim 6.

9. The pharmaceutical composition of claim 8, wherein said compound is the compound of claim 7.

10. Use of the compound of claim 6 for the manufacture of a medicament comprising a compound according to claim 6 for the treatment of hyperglycemia in type II diabetes.

11. The use of claim 10 wherein said compound is the compound of claim 7.

12. A compound according to claims 6 or 7, for use as a therapeutic active substance, in particular for the reduction of hyperglycemia in type II diabetes.

13. The novel crystals, processes, compounds, compositions and uses as hereinbefore described.

14. A process according to Claim 3 or 4 further comprising the step of freezing the crystals.

15. A method of identifying a ligand that binds to the allosteric site of Glucokinase comprising analysing the structure co-ordinates of a co-crystal according to Claim 1.

16. Use of a co-crystal according to Claim 1 or a crystal according to Claim 2 in the identification of a compound which activates Glucokinase.

17. Use of a co-crystal according to Claim 1 or a crystal according to Claim 2 for elucidating the structure and function of a Glucokinase.

18. A compound according to Claim 6 or 7, or a composition according to Claim 8 or 9, for use in a method of treatment of human or animal body.

19. Any novel feature or combination of features described herein.

Application No:	GB 0229456.9	**Examiner:**	Dr Rowena Dinham
Claims searched:	1-5 & 14-17; and 12, 13, 18 and 19 (in part)	**Date of search:**	16 June 2003

Patents Act 1977 : Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance
A, P		*Protein Science*; Vol 11, pp 2456-2463 (2002). Tsuge *et al.* "*Crystal structure of the ADP-dependent glucokinase...*" See entire document, especially Results and Discussion "*Overall strucure*"
A		*Structure*; Vol 9, pp 205-214 (2001). Ito *et al.* "*Structural basis for the ADP-specificity of a novel glucokinase...*" See entire document, especially Results and Discussion "*Crystal structure of* T. lioralis *glucokinase*"
A		*Diabetes*; Vol 48, pp 1698-1705 (1999). Mahalingam *et al.* "*Structural model of human glucokinase...*" See entire document, especially Results "*Overall model and comparison with previous model and hexokinase structures*"

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.

Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC[V]:

Worldwide search of patent documents classified in the following areas of the IPC[7]:

C12N; C30B; G06F

The following online and other databases have been used in the preparation of this search report:

WPI, EPODOC, JAPIO, MEDLINE, BIOSIS, EMBASE, SCISEARCH, CAPLUS